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BUREAU OF HYGIENE AND TROPICAL DISEASES.

TROPICAL DISEASES BULLETIN.

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SUMMARY OF RECENT ABSTRACTS.*

VII. HELMINTHIASIS.

(*Continued from* p. 578.]

Ankylostomiasis ; Infections with Trichostrongylus, Strongyloides and Ascaris.

As a result of the study of an experimental infection with 50 infective larvae of *Necator americanus*, PALMER (p. 98) concludes that hookworm eggs are so unequally distributed in formed stools that the egg count from a random sample does not give a reliable estimate of total egg content. The count of a sample of a homogeneous water suspension of the whole stool is, however, reliable. Egg counts should preferably be expressed as the number per cc. of stool rather than as the number passed *per diem*, because the daily egg output varies more than the egg content per cc.

SAWITZ (p. 771) has tested the buoyancy of certain nematode eggs by means of solutions of different strengths of zinc sulphate. *Enterobius vermicularis* eggs float in a solution of specific gravity 1·115, and at sp. gr. 1·180, 70 per cent. are present on the first cover slip used in a D.C.F. process. *Trichuris trichiura* eggs float at 1·150, and 52 per cent. of eggs are present on the first cover slip at 1·180. *Ancylostoma caninum* eggs float at 1·055, and 87 per cent. are present on the first cover slip at 1·150. LANE had previously noted that a specific gravity of 1·150 is necessary for floating human hookworm eggs. EGAN (p. 463) describes a simple floatation technique for demonstration of hookworm eggs in faeces ; a saturated salt solution is used, without centrifugation.

BROC and CALO (p. 473) refer to the cardio-vascular effects of hookworm infection, which are held to be caused by the anaemia and by toxins from the worms. BROWN and OTTO (p. 99) note that eosinophilia is associated with acute or recent infection with hookworms, but disappears, or is decreased, in cases of long-standing debilitating hookworm disease. AGUIAR (p. 707) considers that there is some clinical evidence to support the view that hookworm infection may lead to fatty nephrosis.

* The information from which this series of summaries has been compiled is given in the abstracts which have appeared in the *Tropical Diseases Bulletin*, 1942, Vol. 39. References to the abstracts are given under the names of the authors quoted, and the pages on which the abstracts are printed.

DE SARAM and GUNEWARDENE (p. 570) report a death rate of about 2 per million in persons treated in Ceylon with anthelmintics for hookworm infection. Most of these fatalities were in children. ALLISON (p. 631) suggests the following outline for the treatment of acute carbon tetrachloride poisoning :—removal of all unabsorbed carbon tetrachloride from the intestinal tract, the forcing of fluids by the mouth and intravenously, blood or plasma transfusion, constant study of the blood, and complete rest in bed. The importance of early intravenous administration of calcium and dextrose is mentioned.

PIERAERTS (p. 99) describes, from the Belgian Congo, a syndrome associated with hookworm infection and the consequent deficiency in iron, and with seasonal changes in food. The colour of the skin may change from black to a yellow tint, and the hair may become the colour of rye straw. Normal pigmentation returns as cure is established. There are, in addition, the common signs and symptoms of hookworm anaemia. This condition, known as diboba, is most common between September and December, when the diet of the people consists chiefly of bread made from manioc. Anthelmintic treatment combined with administration of iron achieves remarkable results. [See also VILLEGAS, below.]

HEILIG (p. 569) states that in Mysore cases of general anasarca are common, and that the usual cause is hookworm infection, which must be differentiated from heart failure and nephritis. Cardiac signs of double mitral disease may be present, but there is no dyspnoea or subicteric tinge. In treatment it is necessary to improve the blood condition so that carbon tetrachloride or tetrachlorethylene may be given without risk. This is effected by administration of Blaud's pills, but a minority of the patients require crude liver extract. A diuretic is given, and this treatment is usually continued for three weeks, by which time the haemoglobin has been raised to 35–40 per cent. Anthelmintic treatment can then be given with safety, and generally brings away innumerable *N. americanus*.

NAPIER *et al.* (p. 100) consider that unless the diet is deficient in iron, even a heavy load of hookworms does not produce anaemia. Rice, especially when polished, is poor in iron, and rice eaters cannot meet the demands of blood loss or pregnancy. The authors conclude, from their investigations, that anthelmintic treatment alone is of little immediate value as regards anaemia in these people, but in anaemic patients a return of haemoglobin to normal may be achieved with iron alone, but cannot be maintained unless the worms are removed. It is not justifiable to treat a patient with a very low haemoglobin level by anthelmintics before iron has been administered. Two courses of ferrous sulphate or ferrous ammonium sulphate in daily amounts of 18–44 grains, each course lasting three weeks, are given in severe cases, and 4 cc. tetrachlorethylene are given in the interval. The anaemia of hookworm infection is due mainly to blood loss, but there may be failure of absorption as a result of intestinal mucosal dysfunction. Very similar views are expressed by ANDREWS (p. 772), who emphasizes that, in the southern United States the primary object in hookworm control should be to detect, prevent and control the disease rather than the subclinical infection. Where iron and protein consumption is adequate, infection will generally not lead to clinical symptoms whatever the worm burden, but where iron and protein consumption is low, chronic anaemia will occur whether hookworm infection is present or not. Hookworm disease is more likely, and more severe, where worm burdens are high

and iron and protein consumption low. The intensity of infection and the diet of the people must therefore be studied. In treatment he advocates a preliminary course of iron in severe cases and a course of iron, after administration of anthelmintic, in moderate cases. In communities in which sanitary reform is difficult, he advises two courses of treatment during the cold months, when the soil does not contain larvae. Tetrachlorethylene is the drug used.

TUCKER and CHISOLM (p. 858) report a great decrease in the incidence of infection with *Necator americanus* in Tennessee since the 1913 survey made by the Rockefeller Sanitary Commission. This reduction is related to improvement in education, sanitation and economic conditions, and the present incidence of disease is much higher among people who do not possess approved sanitary facilities than among those who do. A considerable reduction of the incidence of *Ascaris lumbricoides* infection has also taken place. SAPERO (p. 472) shows that in recruits for the United States Navy drawn from the southern States between 1918 and 1925 the discovered incidence of infection with *Necator americanus* was 23 per cent. After the hookworm campaign in the south the incidence fell to 0·72 in 1932, but recently examination by simple smear gave positive results in 11·3 per cent., and by the Willis floatation method in 21 per cent. Infection was less frequent in coloured men than in white. The average percentage of haemoglobin in the infected was 76, and in the non-infected 83. These findings, in a selected group, indicate a serious situation in the southern States.

PESSOA *et al.* (p. 473) have investigated hookworm infection in São Paulo. They used the Stoll-Hausheer method for egg counts, comparing it with simple smear and with the number of worms recovered after treatment. They note that this method does not detect light infections. In treatment, tetrachlorethylene was found to be fairly effective in doses of 3–4 cc. for adults, the only toxic symptoms being those of dizziness or drunkenness. When Ascaris eggs were present, oil of chenopodium was combined with a reduced dose of tetrachlorethylene. The results indicate that the drugs are more efficient if used in conjunction with a saline purge than if given in castor oil. A single treatment with tetrachlorethylene reduced the number of Necator eggs by about 50 per cent., but two treatments with tetrachlorethylene, or one treatment with carbon tetrachloride, reduced the number by about 80 per cent.

In a town near São Paulo the incidence of *N. americanus* infection was high, especially in girls, and heavy infection with Ascaris, Trichuris and other parasites was found. Hookworm larvae were found in the soil round only one of six schools examined and in soil round only one of six home privies. Eggs of Ascaris, Trichuris and Enterobius were much more common, and these eggs were also found in dust swept from houses. It was noticed that when privies were situated inside the houses the families were not so heavily infected with hookworms as when privies were in the open. The infection rate in children living in homes in which latrines were present was lower (though still high) than the rate in children whose homes did not possess latrines. Summing up this work, the authors conclude that a new hookworm campaign is necessary, and that this should be conducted rather by the school teachers than by members of the sanitary staff. The school should be a centre of instruction on the precautions necessary to prevent the spread of hookworms and other intestinal parasites.

In a discussion of campaigns for the reduction of hookworm infection, GARCIA (p. 96) mentions the disadvantages of dispensaries, the chief of which is that the dispensary does not usually influence enough people. He emphasizes the value of the method adopted by SMILLIE in the Province of Corrientes [Argentina] in 1922, and continued thereafter. This consists of treatment of the sick, which should be repeated annually in districts where latrines are rare and where, therefore, co-operation by the inhabitants is poor. Treatment should be combined with propaganda for the construction of latrines, and where latrines are being built, three treatment courses should be given, during which time it may be hoped that latrines can be installed in about three-quarters of the houses. By such means, directed by the Penna Institute, the numbers of sick in the Province have been reduced, and the capacity for work increased. Certificates may be issued to those persons who have been cleared of the worms.

MILLSPAUGH and SOMPAYRAC (p. 774) describe creeping eruption due to *Ancylostoma brasiliense*. Treatment may be by ethyl chloride spray or by the galvanic cautery after local anaesthesia.

By means of a special technique BUCKLEY (p. 97) has demonstrated, in infective larvae of *Ancylostoma caninum*, positive geotropism at temperatures of 11–14°C., and negative geotropism at temperatures of 21–22°C. These tendencies were present whether the larvae were in light or darkness.

In pointing out that the eggs of Trichostrongylus are rather larger than those of hookworms, with which they may be confused, MAPLESTONE (p. 775) notes that infection with Trichostrongylus is widespread in India ; he has found it in 9·1 to 25 per cent., according to season, of workers in Bengal tea gardens. The species concerned is probably *T. colubriformis*.

TOMITA (p. 101) describes the local symptoms caused by penetration of the skin by larvae of *Strongyloides papillosus* amd *S. fülleborni* ; the latter, but not the former, is able to infect man, and eggs or larvae may be found in the faeces from 16 days to 11 months after infection. BODON (p. 101) reports two cases of infection with *Strongyloides stercoralis* acquired in Italy ; rhabditiform larvae were found in the stools. In one patient this infection apparently gave rise to abdominal symptoms for which the gall bladder and the appendix had been removed.

In Samoa, WILSON (p. 872) found infection with *N. americanus* in 18 per cent., with *A. lumbricoides* in 86 per cent., and with *T. trichiura* in 71 per cent. of the natives, who live in coastal villages. He points out that defaecation into the sea covering the flat coral shelves is the common practice, and that the gentle movement of the sea on these shelves is not sufficient for rapid removal of débris. The eggs of Ascaris and Trichuris sink in Samoan sea water, and development of the embryo within the egg can take place in sea water. He has found live Ascaris and Trichuris eggs in this water, in considerable numbers. He points out, furthermore, that the Samoans make a practice of dipping food into sea water, instead of using salt in the ordinary way, and that after heavy work and consequent loss of salt by sweating they drink a mixture of coconut milk and sea water. Transmission in this manner may account for some part of the high infection rates for these two worms.

VILLEGAS (p. 707) describes a condition in Colombian children infected with Ascaris, which is characterized by cachexia, anasarca and pellagroid lesions, with bleeding of the gums. This is observed in poorly

nourished children. Treatment with anthelmintics and vitamins usually fails, and the case mortality rate is 80 per cent. The author claims good results from the administration of nux vomica, eight drops [presumably of the tincture] daily for 2 weeks, and states that the general condition improves and that large numbers of the worms are eliminated ; appetite is regained. After 3–5 days of this treatment, 4 drops of volatile oil of chenopodium are given in 13 gm. castor oil. A good diet is part of the treatment, which is stated to have produced permanent cure in all cases. [Readers will note the similarity between this condition and those described in West African children under the names of diboba [see PIERAERTS, above], mbwagi, kikuba, kibengi, katoto, buaki (this *Bulletin*, 1939, Vol. 36, pp. 912, 913 ; 1940, Vol. 37, p. 522). Malnutrition seems to be the principal factor, but in West Africa ankylostomiasis appears to play a part, and infection with Ascaris is not, apparently, important there.]

LIU and WONG (p. 476) record the case of a man who, for 20 years, had passed *Ascaris lumbricoides* at intervals *per urethram*. There was a fistula between the small intestine and the bladder.

HALA (p. 571) reports that a child passed a large number of Ascaris after treatment (for pneumonia) with sulphapyridine ; he suggests further investigations of the anthelmintic effect of this drug.

Filariasis.

BONNE *et al.* (p. 184) describe in detail the appearances of the adult male and female of *Wuchereria malayi* ; their findings correspond very closely with those of RAO and MAPLESTONE. The principal features are set out in the original summary.

WOODMAN and BOKHARI (p. 188) have reported, for the first time, the occurrence of *W. bancrofti* in the southern part of the Sudan. There were very few cases, but the diagnosis was amply confirmed.

SAUNDERS (p. 182) refers to the curious fact that although filariasis is very common on the island of St. Croix, it is very rare on the island of St. Thomas 40 miles away ; *Culex fatigans* is common in both. The reason for this difference is obscure. The people of St. Croix are mainly agriculturists, those of St. Thomas are town dwellers not engaged in agriculture, but there are probably other factors which, if properly understood, might lead to simple measures of control in St. Croix.

YOSINO and NAKASATO (p. 183) report a heavy incidence of filariasis in the Yaeyama islands to the east of Formosa.

IYENGAR (p. 477) reports that *Anopheles philippinensis* is the vector of *W. bancrofti* in a rural area of Bengal, in which province filariasis is usually an urban disease transmitted by *Culex fatigans*. Malaria was also present in the rural villages, and *A. philippinensis* was found to be the vector of this also ; in one specmen both infections were found, and it therefore seems probable that this mosquito can transmit both diseases at the same time.

HU (p. 708) has found infective larvae of *W. malayi* in *Anopheles hyrcanus* var. *sinensis* and *Armigeres obturbans* which had been fed on infected patients. The former is the better carrier, but *Armigeres obturbans* is thought to be capable of some transmission in the lower Yangtze region, where it is one of the commonest household mosquitoes. *Aëdes albopictus* did not show infective larvae after feeding on infected persons.

MENON and RAMAMURTI (p. 477) have investigated the escape of infective larvae from the proboscis of *C. fatigans*, and their entry into the skin of the bitten host. Warmth of about 36°C. stimulates the larvae to escape, but they do not penetrate unbroken skin.

DHAYAGUDE and AMIN (p. 707) comment on the absence of records of filarial lesions of the spleen in the post-mortem reports of a Bombay hospital, and describe their findings in the examination of 11 spleens at that hospital, all of which showed lesions readily detected by the naked eye and proved microscopically to be of filarial origin. Histologically these swellings were granulomata, and microfilariae, subsequently identified as *W. bancrofti*, were found in each. Six of the spleens were normal in size, two were smaller than normal and three were enlarged.

RAO and SUKHATME (p. 185) show that there is an annual increase in the incidence of filarial lymphangitis in Calcutta during the monsoon period July to September.

EARLE (p. 571) reports good results from the use of sulphapyridine in certain complications of filariasis, such as lymphangitis, in Nauru. Myositis and " filarial abscess " were not influenced by the drug. He (p. 572) states that the good results in lymphangitis probably indicate that the complication is due to secondary streptococcal infection.

On page 186 is an account of a discussion on surgical complications of filariasis. The details cannot be further abstracted, but it may be noted that RAY regards the lymphangitis as due to the direct effect of the worms, though in a large number of cases there is superadded pyogenic infection ; in treatment, sulphanilamide has been successful even when no secondary streptococcal infection was present.

JUNGE (p. 873) describes the methods he adopts in the operative treatment of elephantiasis of the leg. Details may be found in the original abstract, which cannot usefully be further condensed. The object of treatment should be thorough removal of inflamed proliferative tissue and the creation of new lymph channels ; the latter is achieved by making numerous windows in the fasciae covering the muscles, through which silk threads are passed to act as wicks.

FAUST *et al.* (p. 189) have found a single adult male heartworm in the inferior vena cava of an aged negress in New Orleans. No microfilariae were present. The specimen differed from other species of Dirofilaria and is named *Dirofilaria louisianensis* n. sp. Reservoir hosts must exist, but are not known.

BROWN and SHELDON (p. 190) have found that a combined course of sulphanilamide and Fouadin, continued for 10 days, is effective against *Dirofilaria immitis* in dogs. Five dogs were rendered free of the microfilariae, and in the sixth the count was reduced 96 per cent. In four no adult worms were found at autopsy ; worms, some disintegrating, were found in the other two, but no larvae were present in the female worms examined.

WOODMAN and BOKHARI (p. 188) note that in the Sudan infection with *Loa loa* is found in 15–20 per cent. of the population. Larvae were found in *Chrysops distinctipennis*, though development was slow ; no other vector was found. A description of the microfilaria is given, together with an account of the lesions produced by the infection in man. The authors doubt if there is any drug which will destroy microfilariae of any species and spare the host [but see BROWN and SHELDON above].

NETTEL (p. 572) discusses the localization of nodules in onchocerciasis and emphasizes the importance of a thorough search of the

external auditory meatus. The seriousness of this localization is shown by the fact that of 40 persons suffering from filarial blindness, all had periauricular nodules.

ELLIOTT (p. 778) discusses the clinical aspect of dracontiasis, pointing out that if the worm is deep, or is burrowing along fascial planes, a misdiagnosis of deep cellulitis, myositis, periostitis or even sciatica may be made. He has had success in treatment by means of local injections of phenothiazine, emulsified in olive oil and adeps lanae [in a strength, presumably, of 1 gm. in 20 cc.]. The warmed emulsion is injected at points along the track of the worm after local anaesthesia has been induced, and the sites of injection are firmly massaged. The author claims that no ill effects were seen with doses of 2 gm. phenothiazine given weekly for four weeks. After the injections the worm can be withdrawn in the usual way.

JOB (p. 633) has found that glassfishes of the genus Ambassis feed voraciously on Cyclops. They are found in India in both standing and running water, and may be useful in the biological control of guinea-worm disease.

Enterobius and Trichinella Infections.

JONES and JACOBS (p. 192) show that almost 70 per cent. of eggs of *E. vermicularis* survive for 48 hours when kept in moist, cool air, but that the survival rate is only about 10 in dry, cool air, and is *nil* in dry, warm air. The value of dry atmospheres and high temperatures in control is indicated.

CRAM (p. 191) refers to investigations on Enterobius infections carried out in white and negro families. The results have made apparent the frequency of infection of several members, or whole families, and this fact is of the greatest importance in treatment and prevention. In almost half the white families all the children were infected, and in about half of them one or more adults were also infected.

CRAM *et al.* (p. 191) point out that Enterobius infection is liable to be extremely prevalent in institutions, such as schools, orphanages or mental hospitals.

HILLMAN (p. 877) describes the clinical picture which may be occasioned by infestation of the appendix by *Enterobius vermicularis*. The usual history is of recurring attacks of appendicitis of a mild type, but the picture varies greatly and the condition often cannot be differentiated from acute appendicitis. As a rule in the appendix there are no inflammatory changes and no characteristic pathological picture. In young girls with this syndrome, Enterobius infection should be suspected. ASHBURN (p. 634), moreover, has found that Enterobius is present as often in normal appendices as in those which show chronic inflammation, and more often than in those acutely inflamed. He concludes that this worm is not aetiologically related to appendicitis.

OELKERS and ZESSLER (p. 709) have tested various anthelmintics on Enterobius larvae kept alive *in vitro*. Their resistance is usually high; santonin in saturated solution does not kill them and filmaron, ascaridol and pyrethrin may have no effect even after long periods. Certain thymol derivatives and ethereal oils have proved relatively lethal.

MILLER and ALLEN (p. 781) report on phenothiazine in the treatment of Enterobius infections, noting that there were some toxic effects. They conclude that this drug is probably more effective than gentian

violet, but before recommending its use for children they advise that further study should be made of its haemolytic and toxic properties.

MAPLESTONE and BHADURI (p. 782) have found *Trichinella spiralis* in a cat in India ; this is the first authentic record of this parasite in India. They discuss the life history of the worm, its hosts and the difficulties in prevention of human infection.

LEVIN (p. 193) calculates that larvae of *Trichinella spiralis* enter the muscles of rats (infected by introduction of larvae into the stomach) from the 6th to the 12th day after infection, though adults are found in the intestine up to the 16th day.

WYRENS *et al.* (p. 194) record the finding, in muscle tissue, of cysts of *T. spiralis* during microscopic examination of tonsils, thyroid tissue and other material from patients from whom no history suggestive of trichiniasis could be obtained.

DAMMIN (p. 194) found Trichinella larvae in 5 cc. of blood drawn from the brachial artery of a man 16 days after he had eaten uncooked pork and in whom symptoms suggestive of trichiniasis had developed. This procedure is advised for diagnosis. The patient developed a positive Widal reaction, and gave a delayed positive intradermal test to Trichinella antigen.

BEESON (p. 196) gives a good account of the signs and symptoms of trichiniasis, details of which may be found in the original abstract. He notes that search for the adult worm in the faeces is usually a waste of time, but that larvae are often to be found in the sediment from 5 cc. of blood laked in 50 cc. of water and centrifuged. After the third week, biopsy of muscle is useful. Eosinophilia may reach 40 per cent. in the second and third weeks and may persist for a year. He refers to the intradermal and precipitin tests described by MCNAUGHT *et al.* below. A positive Widal reaction may be present in the acute stage [see DAMMIN above].

DELLA VIDA and DYKE (p. 197) describe the blood changes in trichiniasis. There is leucocytosis with peaks in the third and eleventh weeks after the onset of symptoms, and during these waves the eosinophils are greatly increased.

MCNAUGHT *et al.* (p. 194) describe the procedure for the preparation of antigen for cutaneous and precipitin tests for trichiniasis ; the details may be found in the original abstract. The intradermal test, performed with a saline control, shows, in positive cases, an immediate reaction consisting of a weal surrounded by a zone of erythema, or a delayed reaction which reaches its maximum in 24 hours and appears as a swollen, red area 1–3 cm. in diameter. Most patients in the acute stage give the immediate reaction ; the delayed type occurs in early stages and in long-standing, quiescent cases. The precipitin reaction may be obtained after one hour in a water bath at 37·5°C. Both tests may give positive results years after the initial infection.

MAUSS (p. 572) states that the immunologically active fraction of trichinous rabbit serum is the globulin, and especially the euglobulin, fraction. *Charles Wilcocks.*

RABIES.

A REVIEW OF RECENT ARTICLES.—XXXIX.*

i.—*Virus.*

KLIGLER and BERNKOPF[1] have made some interesting observations in experiments to ascertain the localization and dissemination of virus, following infection by various routes, in normal and immunized mice. The neurotropism of the virus of rabies was established in the early studies on the disease and a considerable amount of evidence has accumulated now to support strongly the view that the propagation of the virus in the body is along nerve paths only. This evidence is not limited, as the authors suggest, to observations made on the localization of the virus in the tissues at the time of death, or to observations made in histological studies only. Nevertheless, it must be agreed that much of the experimental evidence is based on observations following upon inoculation of the virus directly into nervous tissue, whether central or peripheral, and on studies on the effects resulting from resection of nerves before or after such infection.

In the first series of experiments of the present authors, groups of mice three weeks old were infected intraperitoneally or subcutaneously with 0·5 cc. of a 1 : 50 suspension of virus-infected mouse brain and at stated intervals two of the infected mice were killed and various tissues were examined for the presence of virus, by inoculation of suspensions intracerebrally into three mice. In a second experiment the mice were infected subcutaneously, one group in the hind and the other in the fore limb with 0·2 cc. of a 1 : 20 brain suspension. Eight experiments were made with minor variations but fairly uniform results. Although not mentioned in the protocols, other mice were inoculated intramuscularly but the dose of virus suspension is not given. The mice remaining after the lapse of 120 hours were left as controls and all of them died " of typical infection " or " with typical paralysis." It is not stated whether a " street " or " fixed " strain of virus was used in these experiments. The virus inoculated intraperitoneally into mice was usually demonstrable during the first six hours in the peritoneal washings, the mesenteric, axillary and inguinal lymph glands, in the liver and spleen, but was no longer demonstrable after 24 hours in these tissues. No virus was demonstrable in nervous tissues in the early periods but it was detected from 72 hours onwards in the cord and other parts of the c.n.s. The authors state that " after peritoneal infection the cervical cord is always the first segment invaded, thus indicating some pathway of predilection of the virus from the peritoneal cavity to the cord " and that " the nerve invasion takes place in the peritoneal cavity and not in the glands." [This may be true, but their evidence does not appear to be conclusive (see Tables I, III and V). In five experiments out of 14 the virus was recovered from the cervical cord from the 72nd to the 96th hour but the results of only four experiments for the examination of lumbar cord are recorded.]

The greater part of the virus inoculated intraperitoneally appears to be destroyed in various glands during the first 24 hours. " The small

*For the thirty-eighth of this series see this *Bulletin*, Vol. 40, p. 195.

[1] KLIGLER (I. J.) & BERNKOPF (H.). The Path of Dissemination of Rabies Virus in the Body of Normal and Immunized Mice.—*Brit. Jl. Experim. Path.* 1943. Feb. Vol. 24. No. 1. pp. 15–21.

amount of virus actually invading the nerves seems to need up to 72 hours for multiplication and extension along the nerve paths before it has reached the cord and is present there in detectable amounts." It is later found in all parts of the central nervous system. The virus was demonstrable at the site of inoculation and, occasionally, in the regional lymph nodes of mice, four to six hours but not 24 hours after subcutaneous inoculation. There was no general lymphatic distribution as in the case of intraperitoneal inoculation, and virus was not detected in the liver and spleen. After 72 hours the virus was detected in the cord, the part first invaded depending on the site of infection. Later on it was found in all parts of the central nervous system.

Virus inoculated intramuscularly was recovered from the site of inoculation within four to six hours, and in one instance only later than this. Virus was recovered from lymphatic glands on two occasions and then only in those proximal to the point of inoculation. No virus was recovered from the liver and spleen. Only after the disease had advanced to the stage of paralysis (seven days) was virus recovered again from the site of inoculation and the lymphatic glands, suggesting centrifugal spread. Mice inoculated in the foreleg showed virus first in the cervical cord at 72 hours and later in other parts of the c.n.s., those inoculated in the hind leg showed virus first in the lumbar cord at 72 hours. It is recognized that young mice are more susceptible to intraperitoneal infection with rabies virus than old ones. Mice three weeks old and three months old respectively were inoculated intraperitoneally with 0·5 cc. of a 1 : 50 suspension of virus, and the organs and tissues were tested for infectivity at intervals up to four days. After six hours the virus was no longer detectable in the liver and spleen and lymphatic glands of either group of mice. It was detected in the cord of the three-weeks-old but not the three-months-old mice examined on the fourth day. However, in older mice which succumbed to the infection, the virus was detected in the cord as in the young mice. The authors believe that the "widespread lymphatic distribution of the virus after intraperitoneal inoculation and its subsequent destruction offer a possible explanation of the relative insusceptibility of older mice to this route of infection," as well as for the better immunizing effect "of intraperitoneal as compared with subcutaneous injections."

In immunized mice (formalin-treated virus) virus inoculated intraperitoneally disappeared more quickly from the peritoneal washings, liver, spleen and lymphatic glands than in untreated mice, if the degree of immunity was sufficient. In these mice and also in immunized mice inoculated subcutaneously in the limbs with virus, if the immunity was not adequate to prevent the virus from reaching the cord, no difference was observed in the rate of spread of the virus to other parts of the c.n.s. in immunized as compared with untreated mice. The mechanism of immunity consists apparently in a rapid destruction of the virus during the first hours after infection.

[The "Wee, sleekit, cowrin', tim'rous beastie" appears to have become the subject of much controversy. Towards the end of last century, BABES reported that mice were susceptible to rabies. REMLINGER in 1904 and GALLI-VALERIO in 1905 showed that they could be infected, even by the subcutaneous route. Perhaps because BABES in 1892 drew attention to the fact that mice could develop the "furious" form of rabies, and recommended that great care should be taken in handling mice in the later stages to avoid being bitten, the mouse was not favoured as a laboratory animal for the study of this

disease. The rabbit, because, even when inoculated with "street" virus, it developed only paralytic symptoms, came to be the animal of choice for the study of this disease and, of course, PASTEUR's classical work was done with this animal.]

Since WEBSTER and DAWSON [this *Bulletin*, 1935, Vol. 32, p. 608] recorded the use of the mouse for the early diagnosis of rabies, it has become increasingly popular in America both for that purpose and for the evaluation of the immunizing power of anti-rabies vaccines [see *e.g.*, HABEL (1940) this *Bulletin*, 1941, Vol. 38, p. 161]. REMLINGER and BAILLY [2, 3] now report their observations on the use of the mouse for the experimental study of rabies. They had read, among others, WEBSTER's paper [this *Bulletin*, 1940, Vol. 37, p. 619] in which it was suggested that the "traditional rabbit" should be replaced by the Swiss mouse in the study of rabies. The present authors failed to find any "Swiss" mice, which the American workers reported to be specially susceptible to neurotropic viruses including rabies, even in Switzerland! As they discovered that this "Swiss mouse" is "not a zoological species" but a strain arising by mutation in a breeding stock in New York, and they could not procure mice from this stock easily, they resorted first to the grey mouse (*Mus musculus*). Later when it became difficult to find the "traditional rabbit" in the markets for experimental purposes, or the price was prohibitive, they used the "banale souris blanche." They come to the general conclusion that the mouse is more susceptible to infection with rabies virus than the rabbit, and equal if not superior to the guineapig in receptivity. The number of animals used in comparative tests was small, and as it is not proposed that only one mouse should be inoculated in making a diagnosis of rabies, it is hardly justifiable to conclude that in some cases a quicker diagnosis could be made in the guineapig than in the mouse, and that in other instances it was a question whether the mouse did not behave like the rabbit and the guineapig. They state that since the incubation period is shorter, and the mouse appears to be more susceptible to smaller doses of virus, *a priori* it would appear to be advisable to employ the mouse if it is pressing to confirm a diagnosis, or if suspect material contains or is likely to contain only a trace of virus. However, they are of the opinion that these advantages are counterbalanced by the shortness of the disease in the mouse and the variability of the clinical picture. In some cases owing to the shortness of the disease mice are found dead and it is necessary to passage and examine the brain for Negri bodies. [WEBSTER, this *Bulletin*, 1937, Vol. 34, p. 677, suggested inoculating six mice with suspected material, killing one animal on the fifth, sixth and seventh days respectively, and examining their brains for Negri bodies and keeping the other three until symptoms developed. SULKIN and WILLETT (this *Bulletin*, 1940, Vol. 37, p. 194), also consider that the demonstration of Negri bodies in inoculated mice is the only dependable criterion for a positive diagnosis, since the clinical manifestations are too variable and indefinite to be of value.] Remlinger and Bailly[3] are of the opinion that the symptomatology in the grey mouse (*Mus musculus*) and the

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[2] REMLINGER (P.) & BAILLY (J.). La souris peut-elle remplacer le lapin dans l'étude expérimentale de la rage? (Premier mémoire.)—*Arch. Inst. Pasteur d'Algérie*. 1940. Dec. Vol. 18. No. 4. pp. 366–373.

[3] REMLINGER (P.) & BAILLY (J.). Les formes cliniques de la rage de la souris blanche.—*Arch. Inst. Pasteur d'Algérie*. 1942. Mar. Vol. 20. No. 1. pp. 1–9.

white mouse is similar and, judging from reports, the behaviour of these mice and the Swiss mouse to inoculation with rabies virus is the same. (JOHNSON and LEACH [this *Bulletin*, 1941, Vol. 38, p. 159] have reported no essential difference in the susceptibility of 10 different strains of white mice to rabies virus.)

As in the guineapig the symptoms are very polymorphic and the authors refer to two main types in the mouse, "Furious" and "Paralytic." Under the general heading "Furious rabies" in the mouse, they describe :—

(*a*) the ordinary classical type, (*b*) the self mutilating form, and (*c*) the pruriginous type. It is important to note that Remlinger and Bailly have apparently observed "furious" rabies both in the grey and the white mouse. [LEACH (this *Bulletin*, 1938, Vol. 35, p. 644) recorded some experiments with the field mouse (*Peromyscus polionotus polionotus*). He reported that they showed a slightly greater resistance to rabies virus than white mice, and were more excitable and difficult to handle. Furthermore some developed "furious" rabies. Some showed early symptoms and recovered but not if the paralytic stage was reached. He stated also that of 5,339 white mice inoculated, none had shown the "furious" type of disease.] Babes's warning has been mentioned already. Galli-Valerio reported that mice could transmit the disease from one to another by biting, and Remlinger in 1905 reported a case of human rabies produced by the bite of a mouse. A word of caution is therefore necessary as to the handling of mice infected with rabies virus and attention is drawn to the possible danger to laboratory assistants during feeding operations. [Another possibility which should be mentioned is the danger of an excitable infected mouse escaping.] The "furious" type of disease, is observed both after intracerebral and after intramuscular inoculation, especially if "street" virus freshly recovered from rabid dogs, is under investigation, and is generally accompanied by some paralytic symptoms which later dominate the clinical picture.

(*b*) The "furious" self-mutilating type is observed after intramuscular inoculation of virus. The animal is crouched in a corner but if disturbed becomes agitated and utters piercing squeals and bites first at the site of inoculation and later the extremities. The mutilating frenzy increases, lasts for about 24 hours, and later paralytic phenomena dominate.

(*c*) The pruriginous type of "furious" rabies develops suddenly and the pruritus may be confined to the point of inoculation or be generalized. If localized, lesions may vary from depilation to a bleeding area. If generalized, the animal scratches itself everywhere. At the same time locomotor effects observed vary from fibrillar shaking of the head and neck to paralytic effects which rapidly gain ascendancy until death ensues.

Under the general heading of the paralytic form the authors describe (*a*) the common paralytic form, (*b*) the hemiplegic type, and (*c*) ascending paralysis (Landry). In addition they describe the remittent form, the pseudo-tetanic or spasmodic form and the "thunderbolt" and "abortive" types.

In general the symptoms are characterized by polymorphism, and while the "furious" type in the mouse is determined above all by unpassaged "street" virus and the paralytic form by "fixed" or passaged virus, there are exceptions.

The authors have not studied the age of the mouse in relation to susceptibility and symptomatology. CASALS [this *Bulletin*, 1941, Vol. 38, p. 160] has, however, made some observations on these points, to which Remlinger and Bailly refer. These latter authors would probably agree that the white mouse has certain advantages for use as a test animal in the diagnosis of rabies and in the estimation of potency of anti-rabies vaccines. The animals are cheap and generally the incubation period is shorter than in other animals, points of great advantage in the diagnosis of rabies by animal inoculation. Although it has been reported in the literature that material diagnosed as positive for rabies by microscopic methods (Negri bodies) has in about 10–12 per cent. of cases led to a negative result in mouse tests, what is more important is that material, which was diagnosed as negative by microscopic methods and even on occasion (although these occasions would not survive a statistical analysis) by rabbit and guineapig inoculation, has resulted in the development of rabies when inoculated into mice in about the same percentage of instances. The disadvantage of the mouse for certain experiments and tests is obvious, and although "furious" rabies in white mice has not apparently been observed in America, it has now been reported by Remlinger and Bailly and precautions should be taken in working with mice. [Personally the reviewer is of the opinion that although the rabbit is more expensive, if the same care was taken in selecting strains of rabbit, such as for example a Dutch-Himalayan cross, breeding them under good conditions and selecting only young rabbits, as is done in the case of mice, then more uniformity in results could be obtained with the "traditional" rabbit. This is seldom done and in many institutes rabbits are purchased at random in the open market or from dealers who have collected them from widely different sources.]

ii.—*Methods of treatment and statistics.*

In the course of previous experiments LEACH and JOHNSON[4] [this *Bulletin*, 1941, Vol. 38, p. 496, and 1942, Vol. 39, p. 591] reported that a single dose of 5 cc. of the commercial chloroform-inactivated anti-rabies vaccine, which they tested when inoculated subcutaneously into dogs, afforded a high degree of resistance to the intramuscular inoculation of rabies "street" virus. Their results, as in the present paper, had been subjected to statistical analysis. The vaccine is a 33⅓ per cent. suspension of brain material from sheep infected with "fixed" rabies virus treated with 1 per cent. chloroform in the cold with periodic shaking for a period of 30 days until non-infective for mice by intracerebral inoculation.

A single lot of the commercial chloroform-inactivated anti-rabies vaccine was tested for potency in dogs 4·5, 10·5 and 16·5 months after preparation (storage at 5°C.). The dose of vaccine administered was 5 cc. subcutaneously as in previous tests. The test for immunity in the vaccinated dogs was the inoculation, in parallel with a similar number of untreated animals, 30 days later, of 0·5 cc. of "street" rabies virus into each masseter muscle. There were at least 30 dogs in each group. The test animals were kept under observation for a period of 90 days. Autopsies were made on all dogs which died.

[4] LEACH (Charles N.) & JOHNSON (Harald N.). Effect of Prolonged Storage on th Antigenicity of Chloroform-Inactivated Canine Rabies Vaccine.—*Amer. Jl. Public Health.* 1942. Dec. Vol. 32. No. 12. pp. 1380–1382.

Their brains were examined for Negri bodies and if the result was negative 0·03 cc. of a 10 per cent. suspension of various parts of the brain was inoculated intracerebrally into four white mice. The results are given in the following table :—

Storage Months	Vaccinated dogs			Control dogs			Statistical* Significance
	Injected	Died of rabies	Percent.	Injected	Died of rabies	Percent.	
4·5	32	2	6	36	20	56	0·0000
10·5	38	4	11	41	27	66	0·0000
16·5	40	6	15	39	25	64	0·0000

*By corrected χ^2 test. Likelihood of getting a difference as great or greater than that observed in the mortality of the vaccinated and control groups by chance alone.

Although there was suggestive evidence that the antigenicity of the product was slightly reduced on prolonged storage, if the control groups are taken into account the differences in results could have resulted from chance alone.

The present regulations governing the marketing of canine rabies vaccines in America, require that the date of preparation be noted on the label and that the expiration date be given as one year from the date of preparation.

From the results recorded in this paper it is evident that the antigenicity is well maintained for a period of one year.

[WEBSTER (this *Bulletin*, 1940, Vol. 37, p. 619) and WEBSTER and CASALS (this *Bulletin*, 1943, Vol. 40, p. 201), in comparative tests made in mice and dogs, have reported unfavourably on the commercial chloroform-inactivated and especially carbolized anti-rabies vaccines which they have examined. They have recorded good results in experiments in dogs with anti-rabies vaccine prepared by inactivating a suspension of the brain tissue of dogs infected with rabies " fixed " virus (Pasteur-Paris-strain), by irradiation with ultraviolet light. Johnson and Leach on the other hand in the papers referred to above have recorded good results with both commercial chloroform-treated (" fixed " virus, sheep brain) and commercial phenol-treated (" fixed " virus, horse brain) vaccines provided that the same concentration of brain suspension, 33⅓ per cent. was employed. It is difficult to make comparisons of the results reported by the two teams as the percentage of control untreated dogs succumbing to the intramuscular test dose is higher in the experiments by Webster and Casals (80–90 per cent.) than in those of Leach and Johnson (55–66 per cent.), and other factors vary.

Although, owing to unfortunate circumstances which have arisen affecting one of the groups of workers, it is not possible at present, it would be extremely useful for the two sets of workers to compare the same vaccines in a parallel series of tests in dogs. It might then become possible to form an opinion as to whether the carbolized and chloroform-treated vaccines under discussion are equivalent to or less in potency than the irradiated vaccine. If it were found that the ultraviolet treated vaccine was consistently superior to the others in protecting dogs, is it not possible that such factors as the use of virus infected dog brain tissue (homologous) and the Pasteur Paris " fixed "

rabies virus strain play a greater part in the results than the method of inactivation of the virus ?]

CHÁVEZ[5] reports that a carbolized " non-virulent " vaccine has been employed for a period of 12 years in the Institute at Santiago, for the treatment of more than 6,000 human patients, with good results. The accidents [*vide infra* under section on post-vaccinal paralysis, etc.] which occurred were slight and only two deaths occurred and these were of patients bitten on the head ; a mortality of 0·03 per cent. In Santiago rabies is endemic and all persons bitten by dogs are treated, but all the 6,038 cases treated belonged to categories A, B and C. If the living dog which bit the patient can be kept under observation, several injections are given, and if nothing happens after 10 days, treatment is stopped. In all other cases the complete treatment is given, if the animal was not observed and even if the examination for Negri bodies gave a negative result. In about 10 per cent. of cases in which no Negri bodies were found a diagnosis of rabies was made by animal inoculations. Four per cent. brain substance is used for the vaccine and this is treated with 1 per cent. carbolic acid for 24 hours at 37°C. ; (*a*) patients with head bites receive 30 doses in 20 days (4·8 gm.), two doses for first 10 days ; (*b*) patients bitten elsewhere 3·2 gm. in 20 doses, one per day ; (*c*) patients with no lesions, 2·24 gm. in 14 doses, one per day.

In 1935 there was an epizöotic of rabies in Santiago ; 1,051 dogs were examined for rabies and in 217 a positive diagnosis was made ; 983 persons were bitten by rabid dogs or dogs suspected of rabies. In 12 years 10,099 animals responsible for bites were examined for rabies and in 857, or 8·4 per cent., the diagnosis was confirmed.

iii.—*Post-Vaccinal Paralysis and other Accidents.*

BÉGUET and HORRENBERGER[6] make observations on the results of an enquiry into the untoward effects observed in certain patients receiving carbolized anti-rabies vaccines. Similar cases have been referred to by others [see BERNARD, LÉPINE, NOURY, and RAYNAL and LIEOU, this *Bulletin*, 1940, Vol. 37, pp. 620–621] and were reported as far back as 1919 by CORNWALL in India [*Indian Jl. Med. Res.*, 1919, Vol. 6, p. 237]. The unpleasant symptoms appear generally after the 10th injection and comprise violent headache, great anguish, loss of consciousness with considerable slowing or stoppage of the pulse and in certain cases an " unpleasant taste in the mouth." They appear about 5 minutes after the inoculation. In most cases there is a more or less rapid return to normal after development of pallor, cold sweats, nausea, vertigo, sometimes with vomiting, and incontinence of urine. In slight cases the patients get up after 10–15 minutes, while in the worst cases in spite of stimulating injections of ether and camphorated oil they do not recover for several hours. The fact that all the cases were in the group of patients treated with carbolized vaccine excluded the possibility of their being due to emotion from undergoing treatment. They are undesirable because

[5] CHÁVEZ (Federico). Vacunación antirrabica humana en Santiago de Chile. Resultados obtenidos con el uso de vacunas fenicadas durante el periodo de 1929–1940.—*Rev. Inst. Bacteriológ. Chile.* 1940. Dec. Vol. 7. No. 1–2. pp. 17–23. With 2 graphs.

[6] BÉGUET (M.) & HORRENBERGER (R.). Enquête sur les incidents observés au cours de la vaccination antirabique par le vaccin phéniqué.—*Arch. Inst. Pasteur d'Algérie.* 1940. June. Vol. 18. No. 2. pp. 179–202.

unpleasant, and when they occur have a bad moral effect on other patients awaiting treatment, but they are transitory and without any sequelae.

The use of carbolized anti-rabies vaccine has become more general of recent years because of its greater simplicity in preparation and transportability, allowing of decentralization of services. Furthermore, such inactivated or "dead" vaccines are reported to be associated with a lesser incidence of post-vaccinal paralysis than others. In order to determine the relative value of this method of vaccination as compared with Pasteur's, the Pasteur Institute of Algiers decided in 1937 to make a systematic test lasting over a period of some years. An equal number of people were to be treated by each method, but the series was interrupted in 1938 because of the incidence of shock observed in the patients treated with carbolized vaccine. At this time 636 patients had been treated with carbolized vaccine. The symptoms described occurred in 25 patients. No symptoms were recorded in 603 patients treated with Pasteur's vaccine.

Although the symptoms were impressive they were of no great gravity, but the authors considered that they were disquieting enough to merit a questionary being sent to other institutes employing carbolized vaccines. Replies were received from 30 different institutes with an average total of 260,000 patients. Fourteen institutes with a total of 140,000 patients reported no incidents on vaccination; the others reported the occurrence of symptoms of shock similar to those described, in the second half of the period of treatment. In compiling the questionary a number of factors were considered, such as the methods employed in preparing the vaccine, the amount of cerebral substance, the fineness of the suspension, the animal employed (rabbit, guineapig or sheep) the purity of the carbolic acid, the rapidity of the injections, the quantity of vaccine injected (1 to 10 cc.) and whether the patients were standing up or lying down during treatment. The possibility that any one of these was responsible was unlikely after consideration of the replies received. Thus the concentration of cerebral substance varied from 1 to 5 per cent. and although all the cases of shock were reported in institutes employing 5 per cent., three institutes with a total of 150,000 patients employed this concentration without incident. Then again, all institutes reporting incidents employed the rabbit, but that at Colombo, treating an average of 20,000 patients without such symptoms being recorded, also employed the rabbit. Various theories have been advanced to explain these cases but no means of avoiding them have been found. Cornwall considered them to be allergic. REMLINGER and PUNTONI advised the authors to employ a special technique to avoid penetration of a blood vessel during injection of the vaccine but this did not affect the issue. Unless there was overwhelming evidence that carbolized vaccines are more efficacious than Pasteur's vaccine the authors are not inclined, in spite of the other advantages of carbolized vaccine, to consider that it is justifiable to incur the risk of such symptoms of shock developing in those undergoing treatment. Chávez (1910) in Santiago [above] has described undesirable symptoms, in a few cases, occurring during treatment with a carbolized vaccine. The first he describes as an allergic reaction observed from the 6th to the 10th day, characterized by erythema, pruritus and local oedema at the site of the injection accompanied by headache and a slight rise of temperature. No suspension of the treatment is necessary. The second

type resembles, in its description, those cases referred to above. There is an intense cephalalgia, vertigo and anguish at the time of making the injection and Chávez explains it by the entry of a small amount of the inoculum into a blood vessel. He also observed what he referred to as graver symptoms in four cases (0·07 per cent. of those treated), *viz.*, paraplegia or paresis of an arm. These four recovered in about two months' time.

PALACIOS and AVENDAÑO[7] discuss cases of post-vaccinal paralysis which occurred in patients treated in their Institute during the years 1940 and 1941. All six cases belonged to Category A, *i.e.* they had been bitten by dogs proved to have been rabid by demonstration of Negri bodies, as in the cases cited, or by animal inoculation tests. There were three cases in 1940 among 2,212 persons treated and three cases in 1941 among 2,180 vaccinated. This gives a frequency rate of 1 : 700 as against the figure of 1 : 9,702 given by the Hygiene Section of the League of Nations as the incidence rate among persons treated by carbolized vaccines during the period 1928–1935. The ages of the patients were 12, 16, 25, 28, 45 and 60 respectively. The amount of nervous tissue injected was 2·16 to 2·56 gm. The authors discuss the symptoms observed in these cases of post-vaccinal paralysis and the various theories as to their possible cause but these are so well known now as not to require mention again here. They draw attention to several points of interest and their own views. They apparently favour the view that since the frequency and gravity of the accidents appears to be in direct relation to the amount of active virus present in the vaccine, it is virus given in the vaccine which is the most important factor. Moreover, cases of post-vaccinal paralysis have been reported in patients who had been treated after being bitten by dogs which were subsequently reported not to have been rabid. They believe that even carbolized vaccines which are described as " dead " may contain active virus. They have found that 1 per cent. phenol inactivated some batches of virus-infected brain tissue suspension in 24 hours while others required 96 hours. They now employ mice and rats instead of rabbits for testing vaccine for infectivity. Although they tested two series of vaccine in this way with negative results they had made no test of all the vaccines which had produced paralytic symptoms. According to the recommendations of KRAUS they mixed 10 strains of " fixed " virus for their vaccine. They found that Negri bodies could be demonstrated in rats and rabbits inoculated respectively with any of the ten strains. They could not demonstrate these Negri bodies in every passage of an individual strain but they suggest that variations of this sort might be associated with a certain increased virulence for man. The authors continue to study the various points which, it has been recommended, merit investigation with a view to diminishing the number of accidents during vaccination. In view of Remlinger's suggestive evidence in experiments on the possible existence of " paralytic " strains, they are paying particular attention to strains of virus used for their vaccine. [There is no evidence as yet that the mixing of strains has any advantage and in fact this policy is less to be recommended, in the opinion of many, than the use of the Pasteur (Paris) " fixed " rabies strain. Probably this holds good in

[7] PALACIOS (R.) & AVENDAÑO (O.). Los accidentes paralíticos del tratamiento antirrábico.—*Bol. Inst. Bacteriológ. Chile.* 1942. Mar. Vol. 1. No. 1. pp. 20–23.

those countries in which the chief biting animal is the dog. The recent observations of KUBES and GALLIA (this *Bulletin*, 1943, Vol. 40, p. 208) in tests in mice, which require confirmation, are of interest in this connexion. They report from Venezuela that they have found immunological differences between strains of virus from cases of paralytic rabies supposed to be spread by bats and strains of virus of canine origin (" Pasteur group "). A vaccine made from the Pasteur fixed-virus strain did not protect mice well against the strains of virus associated with paralytic rabies (bats), although it conferred a good protection against the " Pasteur group " viruses (canine). On the other hand a vaccine made from a fixed strain of virus recovered from cases of paralytic rabies showed, according to them, a " polyvalent antigenic action."] . . . . . *Ian A. Galloway.*

[References to this interesting subject of paralytic accidents following antirabic treatment have been numerous in this *Bulletin* since 1929. See 1929, Vol. 26, pp. 223, 735 ; 1930, Vol. 27, pp. 254, 751 ; 1931, Vol. 28, pp. 252, 750 ; 1932, Vol. 29, p. 603 ; 1933, Vol. 30, pp. 143, 586 ; 1934, Vol. 31, pp. 149, 646 ; 1935, Vol 32, pp. 179, 617 ; 1936, Vol. 33, p. 324 ; 1937, Vol. 34, p. 237 ; 1938, Vol. 35, p. 653 ; 1939, Vol. 36, p. 730 ; 1941, Vol. 38, p. 497. In most of these yet other references are given.—*Ed.*]

JOHNSON (H. N.). **The Significance of the Negri Body in the Diagnosis and Epidemiology of Rabies.**—*Illinois Med. Jl.* 1942. Vol. 81. No. 5. Reprint pp. 19. [Summary taken from *Vet. Bull.* 1943. June. Vol. 13. No. 6. p. 209. Initialled J. E.]

J. reports the results of a series of observations on dogs and foxes with the object of assessing the value of microscopic examination for the diagnosis of rabies. Of 771 dog brains (suspected cases of rabies) examined over one year in Alabama, 690 were positive by mouse inoculation and 623 of them were positive microscopically, *i.e.* 10·5 per cent. of these cases of rabies were Negri negative.

404 fox brains obtained casually and including some from an outbreak of rabies in foxes were also examined. 128 were positive, 116 of which were Negri positive, giving an error of 10 per cent. All the mouse positive and Negri negative cases were foxes concerned in the outbreak.

Brains of vaccinated dogs which died of rabies after natural infection in Alabama were similarly examined. 92 were mouse positive and 14 per cent. of these were Negri negative.

Of 188 dogs which died of rabies during vaccination experiments, 39·7 per cent. were Negri negative, these being mostly dogs affected with paralytic rabies. In the experiments, the period of incubation and the period of clinical illness were the same in both vaccinated and control groups (21 and 2½ days respectively), showing that the vaccination had not even any delaying action against the virus. In this work some evidence was found that Negri body production varies according to the strain of virus.

The article concludes with a useful discussion on the latter and kindred problems.

BRONSHTEĬN (N. I.) & ZAK (O. S.). Sravnitel'noe izuchenie shtammov fiksirovannovo virusa beshenstva nekotorykh pasterovskikh stantsiĭ. [**Comparative Study of Different Strains of Fixed Rabies Virus.**]—*Zh. Mikrobiol.* Moscow. 1942. No. 7. pp. 81–85. [Summary taken from *Vet. Bull.* 1943. June. Vol. 13. No. 6. p. 209. Signed A. MOLDAWSKY.]

The authors investigated the changes which occurred in fixed virus after many years' passaging in different laboratories, applying the same methods of examination to five industrial strains, *viz.*, Moscow, Ivanova, Tomsk, Tbilisi, and Tashkent. Whereas no sharp and essential differences were found in the first four strains regarding M.L.D. and infectiveness by various routes of inoculation for laboratory animals, the Tashkent strain was found to be highly virulent and unstable, thus being unsuitable for use. The Ivanova strain was found to be extremely resistant to drying, losing its virulence only after ten days. 70·6 per cent. of mice immunized by Fermi's vaccine prepared from the Moscow strain survived infection as compared with 16·6 per cent. of the controls. Fermi's vaccine and Phillips' vaccine, prepared from the Ivanova strain, conferred immunization on 81·8 per cent. and 94·4 per cent. of mice respectively, only 9·12 per cent. of controls resisting infection, In a course of immunization lasting for 25 days, immunity in rabbits against not more than 3–5 M.L.D. was set up. From the tenth day the rabbit sera showed the presence of antibodies ; after the 25th day, sera from the majority of the rabbits neutralized 20 M.L.D. in a dilution of 1 : 10. Rabbits immunized with the Moscow and Tbilisi strains in some cases showed a decrease of antibodies towards the 25th day.

KUBES (V.) & GALLIA (F.). Fenómeno de para-inmunidad entre los virus de la encefalomielitis equina y de la rabia paralítica de Venezuela. [**A Para-Immunity Phenomenon between the Equine Encephalomyelitis and Paralytic Rabies Viruses of Venezuela.**]—*Bol. Inst. Investigaciones Vet.* Caracas. 1942. Nov. Vol. 1. No. 3. pp. 81–101. [11 refs.] English summary.

" The immunological relationship between two native heterologous viruses is studied : (1) fixed bovine-rabies virus, and (2) equine encephalomyelitis virus. The resulting para-immunity phenomenon was paid special attention, particularly whether in its appearance there play a part, in addition to virus antigens, the proteinic substances in the products used for immunization. Swiss mice were employed as test animals.

" The studies comprised three parts :

(1) *In vivo* cross-immunity tests.

(2) *In vitro* cross-immunity tests.

(3) Tests on the stimulating action of the proteinic substances, in the vaccines.

" The first part consisted in vaccination of a group of mice against the rabies virus and of another group against the encephalomyelitis virus. Then either group was inoculated intracranially with the heterologous virus in serial dilutions. Non-vaccinated mice, inoculated simultaneously with equal dilutions and in the same way, served as controls.

" The second part comprised serum cross-neutralizations. The required anti-rabic and anti-encephalomyelitic immune sera were

obtained from mice immunized with the same vaccines and in the same way as those belonging to the *in vivo* tests. The test was performed by mixing 3 serial dilutions of either virus with an equal volume and concentration of the heterologous serum. In one instance, the serum, instead of the virus, was diluted serially. Simultaneously, control mixtures were prepared by substituting normal mouse serum for the immune sera. Following preparation, the mixtures were placed in the incubator at 37°C., for three hours, and then injected into mice.

"The third part tended to analyze the stimulating action of the proteinic substances in the vaccines. For this purpose, two simulated vaccines were prepared from healthy, virus-free tissue: anti-rabies vaccine from normal bovine brain and anti-encephalomyelitis vaccine from chick-embryos equally healthy. The rest of the procedure duplicated the one followed in cross-immunity tests *in vivo*.

"The results may be summarized as follows:

"1. No cross-immunity was observed between the native rabies virus, on the one hand, and the encephalomyelitis virus, on the other.

"2. In return, the existence of a slight cross para-immunity, or nonspecific immunity between them, could be established.

"3. The above-mentioned para-immunity (nonspecific resistance) manifested itself in the form of a slight lengthening of life in mice vaccinated against either rabies or encephalomyelitis, when the latter were inoculated, along with unvaccinated controls, with the heterologous virus. Death was retarded, on an average, for one day.

"4. The intensity of the phenomenon has been more or less equal, whether using massive or limited M.L.D.'s of the heterologous virus.

"5. In contrast to what occurred on tests *in vivo*, the mentioned para-immunity was extremely weak or lacking altogether in serum tests *in vitro*. This would suggest that the phenomenon in question bears a greater relationship to tissue than to serum immunity (complete absence or limited quantity of heterologous antibodies in sera).

"6. Para-immunity is due, above all, to the virus antigens contained in the vaccines, since the latter fail to elicit it when the former are absent from them.

"7. However, there are indications that suspensions of brain or chick-embryo from healthy individuals may also have a certain stimulating influence on the phenomenon. This may be thought to be due to the same cellular stimulation that plays a part in the mechanism of nonspecific protein-therapy.

"8. Comparing the para-immunity stirred up by the anti-rabies vaccine with that due to the anti-encephalomyelitis vaccine, the former was found to be more intense. Perhaps this is accounted for by a greater protein content in the anti-rabies vaccine.

"9. The possibility that the slight para-immunity demonstrated herein may comprise all the group of virus diseases is to be considered.

"10. The para-immunity phenomenon, as reported here, has no importance whatsoever in the field, but it may be of some value for the immunological differentiation of viruses in the laboratory."

[See this *Bulletin*, 1943, Vol. 40, p. 208.]

DE BETTENCOURT (A.). Le traitement antirabique à l'Institut Câmara Pestana (1938–1942). [**Anti-Rabic Treatment at the Institute Câmara Pestana, 1938–1942.**]—*Arquivos Inst. Bact. Câmara Pestana.* 1942. Vol. 8. pp. 229–239.

MALARIA.

COVELL (G.) & PRITAM SINGH. **Malaria in the Coastal Belt of Orissa.**—*Jl. Malaria Inst. of India.* 1942. Dec. Vol. 4. No. 4. pp. 457–593. With 2 maps & 1 graph. [18 refs.]

This is a record of three years' observations carried out by a unit of the Malaria Institute of India. Malaria in the neighbourhood of Chilka Lake has been the subject of several previous reports. FRY as long ago as 1912 noted that spleen rates were high in villages on the shore of the lake and that the spleen rates decreased progressively as the distance from the lake increased, facts which made him suspect that *A. sundaicus* was the vector. *A. sundaicus* is the only malaria vector in India that habitually breeds in salt water. This remained a hypothesis till 1937 when Senior WHITE reported the presence of this species on the Chilka Lake [this *Bulletin*, 1940, Vol. 37, p. 741]. The observations now recorded were made in the coastal belt of Orissa from Chatrapur, 16 miles south of Chilka Lake, to Sana Nairi which is situated near the mid-point of the western shore of the Lake. Expeditions to study particular problems were made to other villages near the Lake and in the coastal belt as far south as Vizianagram. The distribution of malaria is patchy. In some villages it is hyperendemic. Severe epidemics may occur in the spring or in the autumn months. Throughout this area *A. sundaicus* appears to be the only vector of importance. It breeds in Chilka Lake, and in tanks, pools, swamps and ricefields that are subject to flooding by salty water. It was found 81 miles south of the Lake in the coastal belt, but never further inland than six miles from the Lake's western shore. The presence of putrefying algae and other vegetation favours the breeding of *A. sundaicus*. If pools and tanks can be kept free from weeds, breeding can be eliminated; this promises to be the most successful method of combating malaria in this area. The optimum range of salinity of water for *A. sundaicus* breeding in this area appeared to be from 600 to 800 parts per 100,000, but salinity appears to be important only in so far as it affects the growth of vegetation.

[A summary does scant justice to the mass of information contained in this admirable report.] *Norman White.*

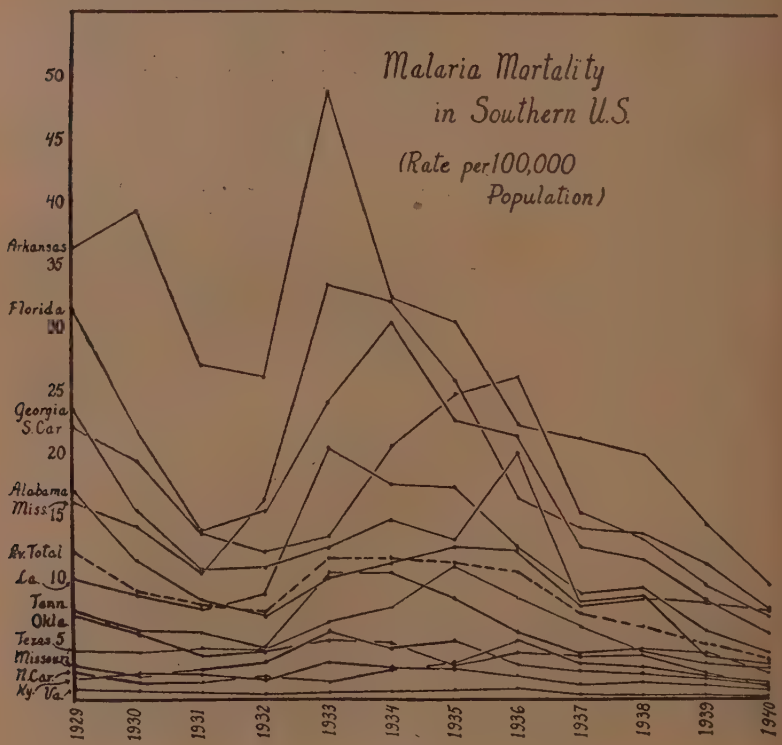
IYENGAR (M. O. T.). **Studies on Malaria in the Deltaic Region of Bengal.**—*Jl. Malaria Inst. of India.* 1942. Dec. Vol. 4. No. 4. pp. 435–446. With 2 figs. [15 refs.]

In the deltaic region of Bengal areas with a high subsoil water level during the rainy season suffer very much less from malaria than do areas with a low subsoil water level. In an endeavour to explain this apparently anomalous phenomenon the author made a study of eight villages around Sonarpur in the 24-Parganas District. No two of these villages are more than four miles apart. In the most eastern village, around which there are numerous ricefields and where the ground is waterlogged for two months during the rainy season, the spleen rate was zero. In the village where the subsoil water was 62 inches below the surface, even during the rainy season, the average spleen rate for the period 1929–1937 was 43 per cent. The other villages are intermediate between these two extremes with regard both to spleen rate and depth of subsoil water in the wet season. Thirteen species of Anopheles were found in this area; *A. philippinensis* is the vector.

Its main breeding season is from July to October. There was a remarkable correlation between the prevalence of *A. philippinensis* and the spleen rate in the different villages. Ponds are the favoured breeding places of this species, and there was no marked difference in the number and variety of such ponds; they exist in all eight villages alike. The manner in which a high subsoil water level acts as a deterrent to the breeding of *A. philippinensis* is not explained; other species of Anopheles breed in abundance in these conditions. It would seem probable that the raising of the water table in the Bengal delta would lower the incidence of malaria. *Norman White.*

FAUST (Ernest Carroll) & DE BAKEY (Lois). **Malaria Mortality in the Southern United States for the Year 1940, with Supplementary Data on Malaria in other States.**—*Jl. National Malaria Soc.* Tallahassee, Fla. 1942. Vol. 1. No. 1. pp. 125–131. With 2 figs.

The malaria mortality in the Southern United States in 1939 was the lowest then on record [this *Bulletin*, 1942, Vol. 39, p. 388]. The year



Graph showing the malaria mortality rates for fourteen Southern States (1929–1940). The broken line represents the average rate for all of these States.

[Reproduced from the *Journal of the National Malaria Society*, Tallahassee, Fla.]

1940 witnessed a still further decline, the average malaria mortality rate of the 14 endemic malaria States being only 3·02 per 100,000. The trend is illustrated in the graph reproduced from this report.

The 5–7 year cyclic increase in malaria deaths which was expected in 1938–1940 failed to materialize. It is possible that the declining mortality since 1938 may be due in part to improved economic conditions of the poorer members of the population. The high rates of 1933–1936 were experienced when the Southern States were feeling the full effects of economic depression. There has been, however, increased antimalaria activity. It is pointed out that the malaria death rate is a direct reflection of *P. falciparum* malaria only, but there is evidence that *P. vivax* malaria has also decreased.

Norman White.

WATSON (Robert Briggs), MAHER (Helen C.) & RICE (Margaret E.). **Observations on Malaria around Lake Wilson, 1934–1941.**—*Jl. National Malaria Soc.* Tallahassee, Fla. 1942. Vol. 1. No. 1. pp. 33–44. With 2 figs.

Lake Wilson, the smallest of the Tennessee River impounded water projects, was formed in 1924 by the completion of the Wilson Dam. It has 135 miles of shoreline. The only shallow water is over the flood plains of small tributary streams. A population of about 4,800 lives within a mile of the lake shore. Such anophelism as occurs is almost entirely due to mosquito breeding in the lake; compared with other Tennessee Valley lakes this anophelism has from 1934 to 1941 been at a low level. In the autumn of each of these eight years blood examinations have been made of 12 to 34 per cent. of the population living within the mile limit. Over the whole period parasites were found in 3·58 per cent. of the bloods examined. Infection rates varied inversely with the distance from the lake. Infection rates were higher for negroes than for whites. There is evidence that cyclic increases in malaria prevalence occur every fifth year. *Norman White.*

EMMEL (L.), GÖLZ (E.) & JAKOB (A.). Elektronenoptische Untersuchungen an Malaria-Sporoziten. [**Electron-optical Observations on Malaria Sporozoites.**]—*Deut. Trop. Ztschr.* 1942. Dec. 1. Vol. 46. No. 23. pp. 573–575. With 3 figs.

In an earlier paper [this *Bulletin*, 1943, Vol. 40, p. 214] some details of the structure of malarial sporozoites as revealed by the electron microscope were given. In the present paper it is noted that further observations have disclosed longitudinal markings or thickenings of the periplast, which are compared with the myonemes of ciliates or gregarines. These markings are more numerous and more conspicuous at one end than they are at the other and are related to the greater mobility of the anterior end of the sporozoite. *C. M. Wenyon.*

LEWIS (D. J.). **A Northern Record of** *Anopheles gambiae* **Giles (Dipt. Culicidae).**—*Proc. Roy. Entom. Soc. London.* (B). 1942. Vol. 11. Pt. 9. pp. 141–142. [Summary taken from *Rev. Applied Entom.* Ser. B. 1943. May. Vol. 31. Pt. 5. p. 88.]

In May 1941, two males and four females of *Anopheles gambiae*, Giles, were bred from larvae collected in river pools about eight miles

north of Wadi Halfa and a few miles south of the Egyptian frontier. The northernmost point from which this species had previously been recorded in the Ethiopian Region is Zeidab (17° 26′ N. lat.). In a paper already noticed, de Meillon discussed its distribution near its southern limit, in the Transvaal, and stated that it is present only in summer in the area with a range of temperature of between 41 and 45°F. and with 0–50 days of frost a year. Wadi Halfa has 0–2 days of frost a year and a temperature range of 60·5°F., the difference between the mean maximum for June and the mean minimum for January (1902–1934).

SWEET (W. C.), FENG (L. C.), CHOW (C. Y.) & HSU (S. C.). **Anophelines of Southwestern Yunnan and their Relation to Malaria.**—*Jl. National Malaria Soc.* Tallahassee, Fla. 1942. Vol. 1. No. 1. pp. 25–32.

In 1940 the International Health Division of the Rockefeller Foundation established a laboratory in Chefang, Yunnan Province, for the study of malaria, in a building previously used by the United States Public Health Service Malaria Commission [this *Bulletin*, 1941, Vol. 38, p. 502]. This report records some of the results of that laboratory's investigations during the first 16 months.

The village of Chefang lies at the northern end of a hill-encircled valley and is the headquarters of a Shan State on the Burma border. It is 2,700 feet above sea level. The valley is about 20 miles long, 5 to 10 miles broad, with many side valleys; it has a population of about 25,000. Rice is the chief crop. There is a rainy season from May to October. The observations recorded all concern this valley.

Twenty-one species, or varieties, of Anopheles were identified: *A. aconitus*, *A. aitkeni*, *A. anandalei* var. *interruptus*, *A. annularis*, *A. barbirostris*, *A. culicifacies*, *A. fluviatilis*, *A. gigas* var. *baileyi*, *A. hyrcanus* var. *sinensis*, *A. hyrcanus* var. *nigerrimus*, *A. jeyporiensis* var. *candidiensis*, *A. kochi*, *A. leucosphyrus*, *A. lindesayi*, *A. maculatus*, *A. minimus*, *A. splendidus*, *A. subpictus*, *A. stephensi*, *A. tessellatus* and *A. vagus*. Of these species *A. aconitus*, *A. annandalei* var. *interruptus*, *A. leucosphyrus*, *A. subpictus* and *A. stephensi* have not previously been reported from Yunnan, or, with the exception of *A. subpictus*, from China. The authors make certain reservations regarding the identity of *A. fluviatilis*.

A. minimus was by far the most prevalent species, three times more prevalent than *A. hyrcanus* var. *sinensis* which previous authors have found to be the most numerous and widespread species in Yunnan. The total number of anophelines dissected was 26,372, of 13 species. The only species found infected was *A. minimus*. Of 18,707 *A. minimus* dissected, 127 harboured oöcysts, and 54 sporozoites. The total number infected was 164, an infection rate of 0·9 for the whole valley and for the whole period of 16 months. There appeared to be no malaria transmission in January and February. Infection rates were highest from August to November. *A. minimus* prefers houses to stables as daylight resting places. It has a marked preference for clear flowing water in which to breed, and its larvae are very rarely found in rice fields. *A. minimus* is the only vector of any importance in this part of Yunnan. *Norman White.*

EYLES (Don E.) & BISHOP (Lindsay K.). **The Microclimate of Diurnal Resting Places of *Anopheles quadrimaculatas* Say in the Vicinity of Reelfoot Lake.**—*Public Health Rep.* 1943. Feb. 5. Vol. 58. No. 6. pp. 217–230. With 4 figs.

The authors selected a number of buildings that were used as daytime resting places by *A. quadrimaculatus*. In some of these as many as 10,000 mosquitoes might be found. They then followed the movements of the mosquitoes out of the shelters at dusk and into them at dawn and endeavoured to correlate these movements with changes in the environment. In the evening the mosquitoes move out chiefly during the 20 minutes after sunset. The only climatic factor that could be correlated with this movement was the fall in light intensity. (The fall in temperature and the rise in humidity takes place an hour or two later in the resting place than in the open.) The influence of light was demonstrated by maintaining artificial light in the shelter. By this means a large proportion of the mosquitoes could be made to remain throughout the evening. The inward movement of mosquitoes in the hours after sunrise is more gradual and seems to depend on the time at which direct sunlight strikes the individual mosquitoes in the open. During the day the temperature in the shelters is lower, and the humidity higher, than outside, the mean differences being 7°F. and 8 per cent. relative humidity. Evaporation (vapour pressure deficit) inside was about two-thirds of that outside; but evaporation from mosquitoes outside would be enormously increased if they were in direct sunlight or exposed to the wind. *V. B. Wigglesworth.*

TEILLARD (M.). *Anopheles hyrcanus* en Provence; morphologie et biologie; gites et refuges. [*A. hyrcanus* **in Provence.**]—*Bull. Soc. Path. Exot.* 1942. Jan. 14 & Feb. 11. Vol. 35. Nos. 1–2. pp. 14–18. [10 refs.]

SIMEONS (A. T. W.). **Economy and Simplification in the Staining of Blood Slides.**—*Indian Med. Gaz.* 1942. Dec. Vol. 77. No. 12. pp. 725–729. With 2 figs.

The authors have tested again the method of staining blood films for malarial parasites advocated by BOYÉ, in which the films are stained first by eosin then by Stévenel's blue and again by eosin. The method has the advantage that the films can be fixed in methylated spirit and that ordinary tap water can be used. Slides are easily stained by immersion in a glass cylinder and the stain in the cylinder can be used repeatedly without deterioration. The total time required for a thin film, allowing one minute for fixation, is under two minutes and for a thick film, allowing one minute for dehaemoglobinization, just over two minutes. Numbers of slides in a suitable rack can be stained at one time. The author states that the results are perfectly satisfactory for all routine clinical work. He also emphasizes the advantages of the rapidity of the method, which leaves little excuse for the administration of quinine to a patient before an accurate diagnosis has been made. In this way much useless administration of quinine can be avoided, an important consideration at the present time. In a footnote to the paper the editor of the *Gazette* says "This method of staining has been tried by us and found excellent for thick films and useful but not ideal for thin films."

[The method, with details for the preparation of the stain, was described in the review of BOYÉ's paper (1940) in this *Bulletin*, 1940, Vol. 37, p. 737.] *C. M. Wenyon.*

TAREYEV (E. M.). [**A Rapid Malignant Form of Malaria of the Tertian Type: (Tertiana Siderans).**] Abstracted from a translation of an article received by the Anglo-Soviet Medical Council, from the Marcinov Central Institution for Malaria and Medical Parasitology. MSS. 5 pp.

Russian authors have recently described in children and young adults a syndrome characterized by acute cerebral symptoms, with death in a few hours. This syndrome has been associated with the presence of *Plasmodium vivax* in the blood, and on this account, and because other cause has not been found, it is suggested that it is a form of *vivax* malaria, for which the name *tertiana perniciosa siderans* is tentatively suggested. Tareyev distinguishes between this condition and the well-known forms of cerebral malaria due to *P. falciparum*. The *vivax* syndrome may arise in primary infections or in the course of early relapses. It is characterized by sudden onset, usually in children apparently perfectly well, with shivering, severe headache, vomiting, convulsions, coma, Cheyne-Stokes respiration and death in 2–3 hours. It is stated that malaria parasites are relatively scanty in the vessels of the brain, in contrast to the usual finding of massive brain infection in comatose malaria due to *P. falciparum* [but in another part of this paper it is stated that the brain is crowded with parasites]. The convolutions of the brain are flattened, the fluid in the ventricles and subarachnoid space is clear and there is no statement that it is in excessive quantity. There is no evidence to indicate that the parasites possess any unusual virulence.

The author attributes the syndrome to anoxaemia of the brain, but does not explain how this is brought about. An allergic condition may be involved, since tuberculous caseation of glands and other so-called para-allergic conditions have been found; persistence of the thymus has been noted. He gives a warning that cases of meningitis and mushroom poisoning have erroneously been diagnosed as *tertiana perniciosa siderans*, and that some cases may resemble heat stroke. Prognosis is very bad, but the patient may be saved by injection of quinine or atebrin. [See also this *Bulletin*, 1943, Vol. 40, p. 436.]

C. W.

DUTT (Probodh Chandra). **A Case of Paroxysmal Haematuria due to Malaria.**—*Indian Med. Gaz.* 1942. Dec. Vol. 77. No. 12. p. 738.

The patient was a child aged four, who had an attack of malaria (mixed *P. vivax* and *P. falciparum* infection) accompanied by the free passage of urine, bright red in colour and containing abundant red cells, with albumin and a few epithelial casts. Other similar attacks occurred, and the haematuria ceased soon after the fever abated under quinine treatment. Urine examined later provided no evidence of renal disease, but the Editor of the *Indian Medical Gazette* suggests that malarial nephritis may have been present. *C. W.*

HARMSEN (H.) & HAUER (A.). Serumreaktionen bei Malaria tertiana. Ein Beitrag zur Frage der Unspezifität der Seroreaktionen. [**Serum Reactions in Benign Tertian Malaria.**]—*Deut. Med. Woch.* 1943. Feb. 19. Vol. 69. No. 7. pp. 147–152. [24 refs.]

The occurrence of non-specific serum reactions is now hardly disputed and only their extent and importance remain obscure. A characteristic group of non-specific reactions is found in malaria. HEINEMANN observed that the Wassermann reaction in malaria is connected with the appearance of parasites in the blood but can occur when they are absent. He believes that a positive W.R. of the cerebrospinal fluid is never caused by malaria. HOHENWERT and KOP showed that a positive W.R. within three months after an attack of malaria is not a proof of syphilitic infection; they found positive reactions even six months after the attack. ASBELOW confirmed Heinemann's observation of a positive W.R. 18 to 24 days after the disappearance of the parasites from the blood. He found the W.R. positive in a high percentage of acute cases of malaria but negative in chronic cases. MEYERSTEIN found the W.R. positive between the fifth and eighth days after the onset of fever in 70 to 80 per cent.; after the tenth day it was less common. He observed that a positive reaction was closely connected with the presence of parasites in the blood. SCHWENKENBECHER regards a positive W.R. as a result of cell destruction with the production of lipoid substances in the circulation. The investigations and views of other workers, especially those of NATALE in Rome, are referred to.

During the period from April 1941 to August 1942, the authors examined the serum of patients suffering from benign tertian malaria and showing no clinical signs of syphilis. Using the Wassermann, Kahn and Meinicke (M.K.R. II) tests they found a positive reaction in 572 out of 1,000 tests. The proportion of positive reactions depends upon how long after the onset of fever the test is made. Many negative results were in relapsed cases. The results are shown in a table which gives the percentages of positive reactions in the three tests. Fresh infections with high fever gave a positive reaction in up to 90 per cent. of cases tested after the fourth or fifth febrile attack. The Kahn test gave most positive reactions and both the Kahn and the W.R. were usually strongly positive while the Meinicke test often gave doubtful or weakly positive reactions. A characteristic of the non-specific serum reaction in malaria is that the W.R. and Kahn reaction appear when the Meinicke reaction is negative or weak. The serum remains positive for some time after the temperature has fallen and the parasites have disappeared from the blood. Patients with strongly positive reactions usually respond well to treatment and a lasting cure follows. On the other hand, in cases with a marked tendency to relapse the serum reaction is usually negative or positive for a very short time only. This is associated with a lack of resistance to the infection, a condition which is sometimes seen also in syphilis and in trichiniasis.

J. F. Corson.

DRENOWSKY (A. K.). Einige Worte ueber die Chinoplasminbehandlung ambulanter Malariakranker. [**Quinoplasmoquine in Malaria.**]—*Deut. Trop. Ztschr.* 1943. Jan. 15. Vol. 47. No. 2. pp. 51–52.

During the malaria seasons of 1940–2, 2,460 ambulant malarial patients were treated by 10-, 15- or 20-day courses of quinoplasmoquine

in doses equivalent to 3 or 4 tablets daily for an adult. Improvement was marked after 3 to 5 days' treatment and there were but few toxic effects, 2·8 per cent. of the patients suffering from alimentary disturbances, 0·2 per cent. from skin rashes and 0·15 per cent. from cyanosis. Relapse rates were 4, 2·7 and 5·9 per cent. for the groups of patients treated for 10, 15 and 20 days respectively. Patients suffering from relapses were treated successfully with 3 tablets daily of atebrin and plasmoquine for 7 or 5 days, followed, after a 3-day interval, by 2 tablets daily of quinoplasmoquine for 5 days. *F. Murgatroyd.*

MUKERJI (B.), GHOSH (B. K.) & SIDDONS (L. B.). **Search for an Anti-malarial Drug in the Indigenous Materia Medica. Part I.**—*Alstonia scholaris*, **F. Br.**—*Indian Med. Gaz.* 1942. Dec. Vol. 77. No. 12. pp. 723–725.

"Careful investigations in the laboratory and in the clinic of the total alkaloids isolated from *Alstonia scholaris* (N.O. *Apocynaceae*), and also of a tincture (1 in 10) made from the powdered bark show that, contrary to popular belief and the earlier records of clinical trials with the drug, *Alstonia scholaris* has little or no demonstrable action in malaria induced in monkeys or naturally occurring in human patients. It cannot therefore be recommended as a substitute for quinine and other cinchona alkaloids."

SOPER (Fred L.) & WILSON (D. Bruce). **Species Eradication. A Practical Goal of Species Reduction in the Control of Mosquito-borne Disease.**—*Jl. National Malaria Soc.* Tallahassee, Fla. 1942. Vol. 1. No. 1. pp. 5–24. With 1 map. [13 refs.]

This is a heartening discussion of the results achieved in Brazil by strenuous effort to eliminate *Aëdes aegypti* and *Anopheles gambiae*. It is a challenge and an encouragement to the rising generation of malariologists. Most public health workers in the tropics, with experience of the unremitting toil and vigilance that is necessary to reduce and keep the density of mosquito vectors of disease below the critical index, have looked upon the total elimination of a prevalent species as an objective impossible of attainment. Experience in Brazil compels modification of this view.

A. gambiae was first discovered in Natal, Rio Grande do Norte, Brazil, in 1930. The anti-malaria campaign that followed was successful in controlling the species in Natal but did nothing to prevent its spread into the interior of the State. The Assú, Mossoró and Jaguaribe valleys were invaded and 1938 witnessed "what may well have been the most severe epidemic of malaria ever occurring in the Americas"; more than 100,000 cases and 14,000 deaths in the first six months. These figures are an understatement; in 1939, 176,000 persons suffering from malaria were treated by the malaria service, which probably failed to reach 25 per cent. of the sick during the epidemic season. The Malaria Service of North-east Brazil was formed in 1939 in cooperation with the International Health Division of the Rockefeller Foundation: it was organized as an anti-*gambiae* service. A discouraging start was an incentive to increased effort. The trained staff eventually numbered 4,000. Simple methods of applying Paris green, both wet and dry, Pyrethrum spraying, and the "flit-umbrella" method of BARBER and RICE [see this *Bulletin*, 1938, Vol. 35, p. 724] of determining the

distribution of species, yielded rapid results. During the second year the area of *gambiae* infestation rapidly diminished. Since January 1941 all anti-*gambiae* measures in Brazil have been suspended ; a cash reward has been offered for the finding of *gambiae*, and a large trained staff searches for the species in the previously infested and adjacent areas ; none has been found.

The history of *Aëdes aegypti* control in Brazil has been equally encouraging. " Local species eradication of aegypti has been accomplished in many of the larger cities and even in entire states, and these have been protected against serious reinfestation for years at a time for but a fraction of the expense previously incurred in maintaining ' safe ' aegypti indices in a few of the larger cities."

The authors suggest that eradication may be equally feasible for these two species in other countries and even for some other species in certain conditions. Among the factors which make species eradication feasible are :—

" 1. Ease in discovering both aquatic and adult forms.

" 2. Efficiency of methods of destroying or sterilizing, permanently or temporarily, all breeding places.

" 3. Opportunity to eradicate the species in a sufficiently large or isolated geographical area so that the periphery, subject to reinfestation from dirty unworked areas, represents but a small fraction of the area worked.

" 4. Demonstrated public health and economic importance of species to be eradicated. Men, money, time and full authority are needed for carrying out species eradication and these are generally available in adequate quantity only for truly serious problems."

Norman White.

Hopkins (G. H. E.). **Modern Methods for the Control of Mosquitoes and Malaria.**—*East African Agric. Jl.* 1942. Vol. 7. No. 4. pp. 212–219 ; Vol. 8. No. 1. pp. 42–46. [Summary taken from *Rev. Applied Entom.* Ser. B. 1943. May. Vol. 31. Pt. 5. pp. 89–90.]

Measures for the control of Anopheline vectors of malaria are reviewed with particular reference to *Anopheles gambiae*, Giles, and *A. funestus*, Giles, the chief vectors in East Africa, and to the author's experience in the application of some of them against these mosquitos in Uganda. They comprise personal protection, measures against adult mosquitos and " naturalistic " and artificial measures against larvae. The subjects dealt with under the first heading are the suitable situation of dwellings (which should be as far as possible from breeding places and, in the case of Europeans and Indians, from those of Africans), mosquito-proofing of houses (which is considered invaluable), bed-nets, mosquito-boots, and the use of a repellent, such as naphthalene and citronella oil in vaseline, for those particularly exposed to attack. Spraying the interior of houses in the evening after the mosquito doors have been shut is recommended against adults, and directions are given for preparing a suitable spray.

The importance of knowing the breeding habits of the local vectors before undertaking naturalistic measures against the larvae is stressed. Those discussed are the organic pollution of water with green vegetation, the introduction of salt water (which must be used only when knowledge of the local conditions is thorough, and is useless against

A. gambiae and *A. funestus*), keeping the water muddy (which is useless against *A. gambiae*), the introduction of larvivorous fish, such as *Gambusia* and *Lebistes*, and of certain plants, shading, the combined shading and drying of swamps by afforestation, which involves enough temporary drainage to enable the trees to become established, and wave action and water flow. Few mosquitos can breed in water that is in constant agitation, and larvae in moving water usually shelter where the flow is obstructed. Knowledge of this principle was applied at Jinja to the control of *A. gambiae* and *A. funestus* breeding extensively for a distance of several miles along the edge of Lake Victoria, in hoof prints in water-logged ground on the shore side of a belt of papyrus and in floating débris on the lakeward side. Beginning in 1931, the papyrus and mudbanks were cut away and much of the material so obtained used to raise the bank well above lake level. A nearly straight shore line of firm steep banks exposed to wave-action resulted. The initial cost was fairly high, but expenditure on upkeep during the ensuing 10 years has been negligible, and breeding along the whole completed stretch has been almost completely eliminated. The same method has recently been applied with complete success to a small lake in Kampala, where *A. funestus* bred extensively.

The artificial anti-larval methods are of two kinds, permanent and temporary. Into the first category fall the filling-in of man-made holes no longer required and of small natural hollows, and the draining of larger natural hollows and seepages, which should not be resorted to unless neither filling nor afforestation is practicable, as the ditches themselves may become breeding places unless they are cemented or underground. Temporary control is effected chiefly by larvicides, and is not approved of if money is available for more permanent measures. The only larvicides dealt with are oil, Paris green dust and cotton-seed " tar " mixed with kerosene (3 : 1). This is proposed as a substitute for oil, which is now difficult to obtain, as Paris green is not considered suitable under East African conditions. Its possible value was suggested by the observation that a stream into which it was discharged from a ginnery contained no larvae for a considerable distance below the outlet pipe. It has an objectionable smell, which may tend to deter ovipositing females. A large-scale experiment with it is in progress [see following abstract].

HOPKINS (G. H. E.). **Cotton-Seed Tar as a Larvicide.**—*East African Med. Jl.* 1943. Feb. Vol. 20. No. 2. pp. 41–45.

An attempt has been made in Uganda to find some efficient mosquito larvicide which would be cheaper than the imported larvicidal oils. A suitable material has been found in what the author calls " gossypix." This is a mixture of three volumes of cotton-seed tar with one volume of kerosene. The tar is a by-product formed during the destructive distillation of cotton-seed in those ginneries which use producer-gas. It is a somewhat viscous, dark brown liquid readily miscible with kerosene. After mixing the " gossypix " is filtered through fine-mesh mosquito-netting and applied with an ordinary oil sprayer. In laboratory and field tests it proved equal in efficiency to commercial larvicidal oils and the cost is estimated at about one-half. The chief disadvantages are that it is somewhat troublesome to prepare and it is available only during the ginning season. *V. B. Wigglesworth.*

KNIPE (Fred W.) & RUSSELL (Paul F.). **A Demonstration Project in the Control of Rural Irrigation Malaria by Antilarval Measures.**—*Jl. Malaria Inst. of India.* 1942. Dec. Vol. 4. No. 4. pp. 615–631. With 1 map & 4 figs. on 2 plates. [17 refs.]

The epidemiology of malaria in the Pattukkottai taluk, Tanjore District of the Madras Presidency, has been described by the authors in previous reports, as have the results achieved in malaria control by spray-killing adult mosquitoes [this *Bulletin*, 1939, Vol. 36, p. 131]. The taluk was free from malaria before the introduction of irrigation in 1933. *A. culicifacies* is the vector. The present report describes four years' work in the control of malaria by measures directed against the breeding of the vector in a group of villages with a population of 3,390 in an area of 7 square miles. In this area there were 3·3 miles of main canal, 4·6 miles of branch canal, and many miles of poorly designed and ill-kept field channels. There were 27 tanks varying in size from a few hundred to several thousand square feet. There were 1,300 wells used for irrigation of ground-nuts between January and June; the canal water was used for the irrigation of rice from June to January. There were 1,900 acres of irrigated land, including 175 acres of swamp and 25 acres of seepage. Countless borrow pits produced *A. culicifacies*.

The malaria control measures employed in undertaking a formidable task included filling and draining, tidying of channels, the use of Gambusia, organic pollution of breeding places, the use of Paris green by dustless and automatic methods, and intermittent irrigation. Some 55,000 yards of filling were used. The measures were applied step by step and with an additional aim of raising the standard of living, by securing better agriculture, better roads, better washing and bathing facilities.

Noteworthy results were achieved. In three villages the spleen rates in the malaria season of 1937 were 48, 54 and 56; in the malaria season of 1941 the spleen rates of these villages were 4, 19 and 11. In a comparable untreated village the corresponding spleen rates were 53 and 57. The fall in the parasite rates during the same period was from 42, 50 and 49 to 0, 10 and 3; in the untreated village it rose from 43 to 48. The total cost of the four-years programme was Rs. 4 : 6 : 0 (6s. 6d.) per head of population: the maintenance cost during a year of observation, after the engineering work was completed, was Re. 0 : 1 : 11 (2½d.) per head. *Norman White.*

ANDREWS (Justin), HOWARD (R. S.) Jr. & TURNER (E. Archer). **Malaria-Control, Ditch-Lining Experience in a South Georgia County.**—*Jl. National Malaria Soc.* Tallahassee, Fla. 1942. Vol. 1. No. 1. pp. 57–67. With 6 figs. on 1 plate & 1 map.

LEGWEN (W. A.) & LENERT (Louva G.). **Circular Joint and Concrete Form Design for Precast Inverts for Malaria-Control Ditch-Lining.**—*Ibid.* pp. 69–82. With 31 figs. on 8 plates.

Both these papers deal with the engineering aspects of ditch-lining, a malaria control measure that has a wide field of application in rural areas and small towns where *A. quadrimaculatus* is the malaria vector. The first paper describes the details of construction of arc-shaped and parabola-shaped invert sections, which can be made with unskilled or semi-skilled labour and at little material cost. The second paper

describes very ingenious slab and joint designs. The slabs can be cast on the job-site; their use reduces the cost of ditch-lining. Constructional details are clearly and fully described in both papers, and the cost of construction in the U.S.A. is given in both cases.

Norman White.

LEGWEN (W. A.) & HOWARD (R. S.), Jr. **The Design and Application of a New Type Automatic Siphon for Malaria Control.**—*Jl. National Malaria Soc.* Tallahassee, Fla. 1942. Vol. 1. No. 1. pp. 83–92. With 12 figs. on 5 plates. [10 refs.]

The automatic siphon described is similar in appearance to the inverted U MacDonald siphon, but modifications in design have succeeded in eliminating the preliminary loss of water before siphonage commences. In this way full advantage can be taken of very small rates of flow. The siphon may be of precast construction or it may be constructed in place on existing dams. Constructional details are clearly described.

Norman White.

WENDEL (William B.). **Respiratory and Carbohydrate Metabolism of Malaria Parasites** (*Plasmodium knowlesi*).—*Jl. Biol. Chem.* 1943. Apr. Vol. 148. No. 1. pp. 21–34. With 8 figs. [17 refs.]

The author has made a study of the respiratory metabolism of *P. knowlesi* in Warburg manometers, with special reference to the relationship between the O_2 consumption and glucose metabolism of this parasite. The observations were made on defibrinated or heparinized whole blood with the addition of various solutions. For the purpose of chemical analysis aerobic and anaerobic incubation was carried out in special Erlenmeyer flasks.

There was marked glycolysis by the parasite in the aerobic experiments and in the case of infected cells, as distinct from normal cells, the process was stimulated by anaerobiosis. Aerobically the initial rise in *p*H of the parasitized blood, due to loss of CO_2, was followed by a fall in *p*H and then by a second slow rise. When glucose was added to the infected blood the *p*H of the medium fell till all the glucose was destroyed or till a *p*H of 5·5 was reached, at which point respiration and glycolysis ceased. The production of lactic acid from glucose was established.

All concentrations of glucose added to the medium reduced the O_2 uptake of the parasites, though the depressing effect of 0·15 per cent. concentration was transient, while the addition of serum prolonged it. Parasitized blood continued to consume O_2 in the absence of glucose. After some hours' incubation, when O_2 uptake was depressed, the addition of Locke's solution + $NaHCO_3$ caused a rise of *p*H in the medium and acceleration of O_2 uptake.

The use of phosphate buffers and neutral salts had a depressing effect on parasite respiration. It was shown that the highest concentration of buffer used did not prevent a fall in the *p*H of the medium though respiration was greatly inhibited, while the lowest concentration of buffer employed was quite ineffective in regulating *p*H but caused a considerable fall in O_2 uptake and decrease in cell volume. Young forms of the parasite were more readily affected than mature forms. It appears, therefore, that phosphate buffer is contraindicated as the

most satisfactory means of controlling the *p*H of the medium. Hypotonic solutions likewise affected respiration and glycolysis adversely, and the parasites are sensitive to ionic as well as osmotic changes.

Evidence was obtained that respiration is only indirectly dependent upon glycolysis. When glucose or lactate was added to parasitized cells washed in Locke's solution, it was found that respiration declined more rapidly after a time with the glucose substrate. About one-half of the glucose destroyed accumulates as lactic acid and neither substance is completely oxidized. When unit numbers of parasites at different stages of growth were compared, ring forms showed the lowest respiratory and glycolytic activity. Only rough correlation of these activities was obtained for parasites at other stages of growth.

A number of conditions favourable and unfavourable to metabolism are given as well as those without effect. Contrary to the results of COGGESHALL [this *Bulletin*, 1940, Vol. 37, p. 670], sulphanilamide was found to be without action on parasite respiration. The author points out that the great glycolytic activity, sensitivity to changes in the composition of the medium and clumping of parasitized red cells, are some of the difficulties associated with the *in vitro* study of *P. knowlesi*.

[In the original investigations in this field by CHRISTOPHERS and FULTON (this *Bulletin*, 1938, Vol. 35, p. 709) the formation of free acid in the medium during incubation of *P. knowlesi* was not established, possibly owing to the use of phosphate buffers, and lactate failed to stimulate respiration significantly. In the present investigation sodium dl-lactate was used, the nature of that used in the original experiments was not stated. It is surprising that, in the present investigation, sulphanilamide was found to have no influence on parasite respiration, in view of the marked prophylactic and therapeutic action of this drug in *P. knowlesi* infections of monkeys as described by COGGESHALL (this *Bulletin*, 1938, Vol. 35, p. 897; 1939, Vol. 36, p. 824, as well as of its activity *in vitro* already referred to).] *J. D. Fulton.*

TRAGER (William). **Further Studies on the Survival and Development in Vitro of a Malarial Parasite.**—*Jl. Experim. Med.* 1943. May 1. Vol. 77. No. 5. pp. 411–420.

In the original paper of this series [this *Bulletin*, 1942, Vol. 39, p. 440] the author indicated certain conditions which favoured the survival *in vitro* of *P. lophurae*. It was then shown that the parasite survived five days, as judged by exflagellation of male gametocytes, or six days if infectivity were taken as the criterion. The period of parasite survival has been considerably extended in the present experiments.

Infected blood was obtained by cardiac puncture of young chickens or ducks, and after centrifugation the red cells were mixed with an equal volume of normal red cells, from the same species of host, in twice their volume of a balanced salt solution, whose composition is given. The basic medium to which the infected cells were added consisted, as previously, of red cell extract from the appropriate host and was made up with definite quantities of serum and the balanced salt solution referred to. In some experiments the medium contained 0·1 per cent. glutathione, and glucose was at times replaced by glycogen. Various growth factors, amongst which calcium pantothenate had a marked influence on survival, were added in sterile aqueous solution to the medium, while chick embryo extract was invariably added in the salt solution.

In each Erlenmeyer flask (25 ml. capacity) 2 ml. of medium was used, and in those experiments in which the medium was changed, one-third to one-half of its volume was removed each time and fresh material at the correct temperature substituted. In other experiments fresh red cells of the avian host were added to the medium in the salt solution every second day. Gentle agitation of the preparation was effected by a rocking machine.

Stained films and red cell counts were made of the contents of each flask at the start of the experiment, and this procedure was followed on succeeding days along with the preparation of a wet film, and suitable dilutions for infectivity tests when required. The exflagellation test was used exclusively in later experiments as a criterion of survival of the parasites. The author notes that material from ducks always had more exflagellating forms than those from chicks, a result which probably depends on the host-parasite relationships.

Under these conditions *P. lophurae* was enabled to survive *in vitro* for about two weeks. In some cases there was a significant increase in male gametocytes and, less often, in total numbers of parasites during the first few days. *J. D. Fulton.*

TRAGER (William). **The Influence of Biotin upon Susceptibility to Malaria.**—*Science.* 1943. Feb. 26. Vol. 97. No. 2513. pp. 206–207.

The author reviews previous work, which shows that the severity of *Plasmodium lophurae* infections in young chickens and ducks is greatly influenced by the level of biotin in the host. Furthermore, at the peak of an acute infection the biotin reaches three or four times its normal value and then returns to normal as the infection subsides. Chickens or ducks, rendered biotin-deficient by a two or three weeks' diet of egg-white [see *Bulletin of Hygiene*, 1942, Vol. 17, p. 646], when inoculated develop infections with parasite numbers which are 50 to 100 per cent. higher than those in control birds. The heavier infections persist for several days longer and more birds die. Chickens which are made only moderately deficient in biotin so that they grow well and appear normal, develop heavier infections than do birds having more adequate supplies of biotin. Similar results are obtained with chickens infected with *P. gallinaceum*. Biotin-deficient ducks injected with *P. cathemerium* do not develop heavier infections than normal ducks but the infections persist for several days longer than in control ducks, while several of the deficient ducks die. It has been shown that the increase in biotin during the course of an infection is not due to the new red cells formed in response to the anaemia produced by the parasites. It is not yet known whether these findings will apply to simian and human malaria, but they indicate that biotin is one substance of known chemical nature which helps to determine the degree of resistance of the host to infection with malarial parasites.

C. M. Wenyon.

LACK (Arthur R.), Jr. **The Occurrence of Intravascular Agglutinations in Avian Malaria.**—*Science.* 1942. Dec. 4. Vol. 96. No. 2501. pp. 520–521.

By using the Knisely quartz rod micro-illuminator, it has been possible to study the pathological changes which take place in the circulation of the wing vessels of canaries during the development of a

malarial infection. There was evidence of leakage of plasma into the tissues surrounding the blood vessels, progressive adherence of white blood corpuscles to the endothelium, increasing agglutination of infected and then uninfected red blood corpuscles in growing clumps and increasing viscosity of the plasma. The circulatory damage resulting from these changes and the developing infection led eventually to circulatory failure and death of the bird. [See also this *Bulletin*, 1943, Vol. 40, p. 584.] *C. M. Wenyon.*

KIKUTH (Walter) & MUDROW (Lilly). Noch einmal: Ueber die Entwicklung der Sporozoiten der Malariaparasiten. [**Further Remarks on the Development of Sporozoites of Malarial Parasites.**] —*Zent. f. Bakt.* I. Abt. Orig. 1942. June 30. Vol. 149. No. 2. pp. 98–101. [12 refs.]

In this paper the authors continue the controversy they had with MISSIROLI on the subject of the early stages of development of malarial sporozoites in birds [this *Bulletin*, 1942, Vol. 39, p. 399]. They again contend, with seeming justification, that Missiroli's claim that the sporozoites are actually sporocysts which undergo extracellular development in the lymphatic spaces in the bird is unfounded. They hold that the sporozoites after injection into the bird enter cells of the reticulo-endothelial system of the endothelium, and there proceed to schizogonic development, as previously described by them.

C. M. Wenyon.

BLACKWATER FEVER.

BURKITT (R. W.). **Treatment of Blackwater Fever.** [Correspondence.] —*Brit. Med. Jl.* 1943. June 12. p. 737.

Burkitt writes that, when treating cases of blackwater fever in East Africa, he was struck by the great restlessness of mind and body characteristic of that disease, and to counteract this gave 8–10 grains of sodium luminal intramuscularly, having been dissatisfied with morphine. In eight cases so treated in the evening, all trace of blackwater had disappeared by the following morning; additional treatment consisted of plenty of fluid containing sodium bicarbonate and glucose by the mouth. There were no recurrences. He now reports that Dr. J. R. GREGORY of Nairobi has had a series of 30 cases, all treated by intravenous injection of 15 grains of phenobarbitone, and all "cured at once." He remarks:—"I have used the unscientific expression 'cured at once' for the express purpose that it gives the picture exactly." *C. W.*

GUPTA (J. C.). KAHALI (B. S.) & GANGULY (S. C.). *Vitex peduncularis*—**an Antihaemolytic Agent.**—*Indian Med. Gaz.* 1942. Dec. Vol. 77. No. 12. pp. 721–723.

In 1921, VAUGHAN reported that aboriginal tribes of Ranchi in India were in the habit of using aqueous infusions of *Vitex peduncularis* in the treatment of malaria and blackwater fever. He treated cases of these diseases himself and suggested that in vitex might be found

active principles which would provide all the powers of quinine without many of the dangers and drawbacks. Later CHOPRA, KNOWLES and GUPTA (1924) tried the drug in malaria but failed to obtain any evidence of activity [see this *Bulletin*, 1924, Vol. 21, pp. 604, 857]. Recently MEASHAM [this *Bulletin*, 1940, Vol. 37, p. 837] employed it in blackwater fever and concluded that it had a definite value. It appeared that this conclusion was based more upon clinical impressions than on actual data, so that it seemed advisable to carry out a pharmacological study, which the authors of the present paper have undertaken. They have found that the addition of vitex, the name used for the infusion of the leaves, to suspensions of washed red blood corpuscles of the rabbit, or its administration intramuscularly or orally, increases the osmotic resistance of the cells and inhibits haemolysis by saponin, acid, cobra venom, bile salts and saline solutions. It is assumed that vitex has some action on the surface of the red blood corpuscles. It is concluded that vitex might inhibit the haemolysis which occurs in blackwater fever and that, as many cases of this condition follow the administration of quinine, it might be advantageous to give vitex before quinine to those patients suffering from malaria who, from the history or appearance, would seem to be liable to blackwater fever. [See also this *Bulletin*, 1920, Vol. 17, p. 306; 1925, Vol. 22, p. 50; 1942, Vol. 39, p. 531.] *C. M. Wenyon.*

TRYPANOSOMIASIS.

LEWIS (E. A.). **Tsetse-Flies and Development in Kenya Colony. Part III.**—*East African Agric. Jl.* 1942. Vol. 8. pp. 74–79. [Summary taken from *Vet. Bull.* 1943. June. Vol. 13. No. 6. p. 215. Signed U. F. RICHARDSON.]

This part deals with methods of tsetse control, and points out that traps, which have been so successful against *Glossina pallidipes* in Zululand, soon deteriorate under tropical conditions, do not attract *G. pallidipes* when the density is low, and seem to be less attractive at some seasons than at others. Local experience in Kenya shows that the creation of an artificial fly concentration by the use of scent baits, etc., is necessary to prolong or increase the efficacy of the traps.

Ruthless bush clearing as a means of controlling tsetse has come to be considered too drastic and costly, but it has been shown that the clearing of barriers is sufficient to prevent extension, and can be used to isolate blocks of infested country in which the tsetse can be dealt with by other methods. Discriminative clearing and densification of bush can be used in some areas to render them unsuitable for tsetse, but the degree of afforestation required by each species has not yet been determined, and often two or more species are concerned in one area.

Game reduction appears to have given very satisfactory results in Southern Rhodesia, but it is doubted whether it would be effective against species which are not so well adapted to game as is *G. morsitans*. Each species and each area present different problems in control. It is suggested that a plan of approach should be adopted which should be sufficiently flexible to allow for modifications and new methods, as research workers discover new means of attack.

McDermott (Walsh), Webster (Bruce), Baker (Richard), Lockhart (James) & Tompsett (Ralph). **Nutritional Degeneration of the Optic Nerve in Rats: its Relation to Tryparsamide Amblyopia.**—*Jl. Pharm. & Experim. Therap.* 1943. Jan. Vol. 77. No. 1. pp. 24–39. With 5 figs. [36 refs.]

Although extensive studies have been made on the general toxicity of tryparsamide, only three studies have been done on its apparently selective action on the optic nerve. Recently Longley and his colleagues produced blindness in monkeys by using very large doses of tryparsamide.

There has been much interest lately on the nutritional aspect and certain observations that have been made have a bearing on the problem of tryparsamide amblyopia. Most of the clinical reports of disease of the optic nerve, associated with abnormal nutritional states, deal with supposed deficiency of the B group of vitamins, either alone or combined with deficiency in vitamin A, while most animal experiments have been made with vitamin A deficiency. The relationship of nutrition to toxic amblyopia has been investigated both clinically and experimentally. It has been shown that large amounts of the vitamin B complex will cure amblyopia caused by alcohol or tobacco even during the continued consumption of large amounts of both. Contrary results have been obtained by different workers in treating tryparsamide amblyopia with thiamin chloride.

Imachi and Maruo found that certain chemical poisons and bacterial toxins caused damage to the optic nerve in rats and that it was most severe in those which were fed on a diet deficient in vitamin A.

From a review of the experimental work the authors of this article conclude that the proper utilization of at least two dietary factors is necessary for the maintenance of the integrity of the nervous system in animals, *viz.*, vitamin A and some part of the vitamin B complex which is not thiamin, riboflavin or nicotinic acid. On account of the apparent importance of vitamin nutrition in disease of the optic nerve and in the prevention of nerve damage due to poisons, they decided to make an experimental study of tryparsamide from this standpoint.

Part I. Vitamin B complex.—Eleven groups of five young rats were given a basic synthetic diet completely lacking in the vitamin B complex. This was supplemented in various groups by crystalline vitamins, desiccated liver or irradiated brewer's yeast. The control diet was the basic diet plus 10 per cent. of powdered yeast. Tryparsamide was given intravenously to six of the groups in doses of 0·1 gm. per kgm. body weight weekly for 10 weeks, and the rats were then killed and transverse sections of the optic nerve examined.

Results.—Degeneration of the optic nerve developed in those rats which were fed on the basic diet without supplements, whether they received tryparsamide or not, but it was more marked in the former group. None of the other groups showed optic nerve degeneration and no obvious evidence of blindness was noted. Rats which had received tryparsamide during a period of clinical vitamin B deficiency but which had been cured subsequently of the deficiency by supplemented yeast, showed no evidence of optic nerve degeneration seven weeks later, although the administration of tryparsamide had been continued.

It would seem that the substance in yeast responsible for the preservation of the nerve is one (or some) of the already isolated members of

the B complex, but is not pantothenic acid alone. The results support WINTROBE's conclusion that the "antineuritic vitamin" is actually two substances, pantothenic acid and pyridoxine.

Part II. Vitamin A.—Similar experiments were made with five groups of five rats with a basic diet completely lacking in vitamin A. Three of the groups received a supplement of cod liver oil in different amounts. Tryparsamide was given to four groups while the remaining group were fed on the basic diet without supplement.

Results.—Advanced degeneration of the optic nerve developed in the rats fed on the basic diet whether they had received tryparsamide or not; it was more advanced in those which had not received tryparsamide, but the difference is thought to be more apparent than real owing to the small number of animals used and to the extensive degenerative changes which made exact measurement difficult. The rats which received extremely small quantities of supplemental cod liver oil also showed a moderate degree of optic nerve degeneration although there were no clinical signs of vitamin A deficiency.

[The observations of D. G. F. MOORE referred to were made in West Africa, not in South Africa, as stated by the authors.] *J. F. Corson.*

TORREALBA (J. F.). Investigaciones sobre enfermedad de Chagas en el Estado Guárico, Venezuela. [**Chagas's Disease in Guárico, Venezuela.**]—*Gac. Méd. de Caracas.* 1943. Jan. 15. Vol. 50. No. 1. pp. 3–4.

This article, though short, is important. Three questions are considered: (1) Examination of Triatomidae in the Roscio district. (2) The first recorded cases of acute Chagas's disease in San Juan de Los Morros, Roscio District. (3) A newly discovered reservoir host in the State.

In 1939 the author captured a large number of *Rhodnius prolixus* and sent them to Professor Brumpt, who was then visiting Venezuela. Every one of the bugs was found to be infected. The author himself later examined other lots and found 48 per cent. infected, but none of *E. maculata, Panstrongylus geniculatus, Psammolestes arthuri* and others. In the hilly regions of La Llanada, Las Glorieta, Garrapata, Los Morros and Guayabal and their suburbs more than half of the people examined were infected with *T. cruzi.*

In the second part the author records two cases, one in a boy of five months, the other in a boy of four years, seen in August 1942. Both were from the suburbs of San Juan de Los Morros.

The fact that *Cebus apella,* the horned Capuchin monkey of South America, is readily inoculable with *T. cruzi* has been known for a long time, but the author in 1941, when examining the blood of one of these animals prior to using it for experiments with malaria, found it naturally infected. This must now be added to the list of natural reservoir hosts. *H. Harold Scott.*

TORANZOS (Lázaro B.), FIGUERERO (Manuel) & BARBARÁ (Luis). Primer caso agudo de enfermedad de Chagas en el Departamento Mercedes (Provincia de Corrientes). [**First Acute Case of Chagas's Disease in the Department of Mercedes, Corrientes Province.**]—*Bol. Sanitario.* Buenos Aires. 1942. July–Sept. Vol. 6. Nos. 7–9. pp. 469–473. With 2 figs. & 1 chart.

The case was a straightforward one in a child of 5 years and 7 months, seen in November 1940. He came to the hospital with Romaña's

sign, swollen left eyelids, oedema and a small haemorrhagic spot. The pre-auricular gland was enlarged and also, slightly, the cervical glands; the pulse was rapid, 110 per minute. The trypanosome was seen in a thick drop preparation of the blood and animal inoculation proved positive. Bayer 7602 (Ac) was given according to the routine recommended by Professor Mazza.

Triatoma infestans caught in the child's residence were examined and one of five was found infected. The course of the illness is not stated beyond the remark that "the oedema of the lids subsided slowly in course of time." Incidentally, the serum was positive with both the Wassermann and the Kahn tests. *H. Harold Scott.*

DENISON (Nadene). **Immunologic Studies on Experimental** *Trypanosoma cruzi* **Infections: I. Lysins in Blood of Infected Rats.**—*Proc. Soc. Experim. Biol. & Med.* 1943. Jan. Vol. 52. No. 1. pp. 26–27.

The serum of rats which have recovered from *Trypanosoma cruzi* infection will produce lysis of the culture forms of this trypanosome in a mean time of 61·3 minutes. The serum from animals which had had the reticulo-endothelial system blocked with trypan blue before being infected did not lyse the culture forms till a mean time of 88 minutes had elapsed. The serum of uninfected animals which had been blocked produced lysis in 153·6 minutes. When the various sera had been inactivated before testing it was found that the organisms were immobilized but not lysed.

In these tests the serum was diluted 1 : 1. If diluted 1 : 10 there was no lysis up to a period of 7 hours in any class of test. In a series of tests with culture forms of *T. lewisi* and *Leishmania tropica* there was no lysis, but motility was rapidly impaired. *C. M. Wenyon.*

SENEKJI (Harry A.). **Immunologic Studies in Experimental** *Trypanosoma cruzi* **Infections: 2. Slide Agglutination and Intradermal Tests.**—*Proc. Soc. Experim. Biol. & Med.* 1943. Jan. Vol. 52. No. 1. pp. 56–59.

The author has immunized rabbits against *Trypanosoma cruzi* infection by injection of killed culture forms followed by injections of living trypanosomes. The serum of such immunized rabbits was collected and tested for agglutinins and lysins against "H" and "O" antigens. The former was prepared by the addition of 0·3 per cent. formalin to a saline suspension of culture forms and the latter by the suspension of culture forms in 90 per cent. alcohol. Agglutination tests were carried out in tubes with various dilutions of the serum of the immunized rabbits and the "H" and "O" antigens. No differences were noted between the two readings. Slide agglutination tests were carried out with an antigen prepared by emulsifying flagellates from cultures of an armadillo strain which was very smooth in salt solution containing 0·5 per cent. phenol. Agglutination, which was very marked in low dilutions of serum, was complete in 3 to 5 minutes. The intradermal injection of cultures into the skin of immunized rabbits produced, after 12 hours, a red papule which increased in size to reach its maximum in 24 hours. Immune serum in a dilution of 1 : 100 lysed the culture forms in two hours.

As a control to the above reactions 100 Wassermann sera were used. They were uniformly negative. The author considers that the slide agglutination test affords a simple method for the diagnosis of experimental *T. cruzi* infections in animals. *C. M. Wenyon.*

Dr. Gustavo LESSA, referring to his paper on the epidemiology of Chagas's disease [this *Bulletin*, 1924, Vol. 21, p. 53] has written to say that the arguments advanced at that time to support the theory that there was an aetiological connexion between goitre and Chagas's disease were not convincing to him, but, on the contrary, that he tried to show their weakness. He adds that the essential purpose of that paper was to give the reasons for his belief in the widespread diffusion of the disease.—*Ed.*

In the section LEISHMANIASIS, below, is included a series of papers dealing with the pharmacology and toxicity of certain aromatic diamidines. These drugs have an interest for workers on trypanosomiasis because of their successful use in this disease.—*Ed.*

LEISHMANIASIS.

WIEN (R.). **The Pharmacological Actions of certain Aromatic Diamidines possessing Trypanocidal Activity.**—*Ann. Trop. Med. & Parasit.* 1943. Apr. 30. Vol. 37. No. 1. pp. 1–18. With 12 figs. [24 refs.]

The compounds investigated were the dihydrochloride salts of 4 : 4′-diamidino diphenyl ether, 4 : 4′-diamidino stilbene, 4 : 4′-diamidino 1 : 3 diphenoxy propane and 4 : 4′-diamidino 1 : 5 diphenoxy pentane. These compounds, which were introduced by the work of YORKE, EWINS, and their collaborators, are important for their therapeutic action in trypanosomiasis, leishmaniasis, and babesiasis. In toxicity experiments with mice, giving a single dose intravenously it was found that the LD 50 (dose causing 50 per cent. mortality) was 0·050 mgm. per gm. for the ether derivative, 0·031 mgm. per gm. for the stilbene derivative, 0·042 mgm. for the propane derivative and 0·028 mgm. per gm. for the pentane derivative. When the drugs were given subcutaneously, the LD 50 was somewhat higher. The symptoms consisted of general depression of the central nervous system, and death resulted from respiratory failure. When repeated sublethal doses were given to young rats, symptoms suggestive of cumulative poisoning developed.

When examined by standard pharmacological methods, the compounds were found to have a depressant action on the circulatory system, which was only partially antagonized by atropine. The fall of

blood pressure which followed intravenous injection of the compounds was prevented or much reduced by a previous injection of calcium; this action seems to be similar to the action of these compounds in sensitizing frog's striated muscle to potassium ions. In this respect the compounds resemble guanidine. Perfusion and plethysmograph experiments in rabbits, cats and dogs showed that the fall in blood pressure was due mainly to peripheral vaso-dilatation. The effects on the heart were small and transitory, low concentrations stimulating it and high concentrations depressing it. The compounds had an ergotoxine-like action and reduced the actions of adrenalin on the blood pressure, uterus, and perfused vessels of the rabbit's ear and the cat's hind limb. Isolated plain muscle of the rabbit's intestine, of the guineapig's uterus, and of the cat's uterus was stimulated by high concentrations; these effects were not abolished by atropine.

F. Hawking.

WIEN (R.), FREEMAN (W.) & SCOTCHER (N. M.). **The Metabolic Effects produced by certain Aromatic Diamidines.**—*Ann. Trop. Med. & Parasit.* 1943. Apr. 30. Vol. 37. No. 1. pp. 19–33. [19 refs.]

This paper reports further investigations on the ether, stilbene, propamidine and pentane aromatic diamidine compounds discussed by Wien above. The compounds affected the blood sugar only in doses which approached the toxic level. The main effect was to produce hyperglycaemia, and the ether derivative (phenamidine) was the least active in this respect. The hyperglycaemia was due partly to increased output of adrenalin from the adrenals. Propamidine produced a subsequent hypoglycaemic condition. Repeated high doses of the diamidine compounds produced marked depletion of liver glycogen, but this may have been due in part to anorexia; fatty degeneration of the liver was one of the main histological changes due to chronic poisoning.

The compounds also acted on the kidneys, as shown by an increase in the blood urea and non-protein nitrogen figures. In some instances the blood urea was raised by doses which did not influence the blood sugar. By subcutaneous injection phenamidine produced less response than stilbamidine, while propamidine and pentamidine produced nearly equal effects. Histologically, the kidneys showed cloudy swelling and fat globules in the cells of the convoluted tubules.

In dogs and rabbits, the serum calcium and potassium levels were both reduced by the drugs within a few hours. No gross changes in the blood picture (guineapigs) were observed unless toxic doses were employed.

F. Hawking.

FULTON (J. D.). **Studies in Chemotherapy. XXXIII.—Toxicity and Therapeutic Action of certain Aromatic Diamidines after Exposure to Light.**—*Ann. Trop. Med. & Parasit.* 1943. Apr. 30. Vol. 37. No. 1. pp. 48–59. [11 refs.]

A previous paper by FULTON & YORKE [this *Bulletin*, 1943, Vol. 40, p. 23] had shown that solutions of stilbamidine (diamidino-stilbene) became more toxic when exposed to sunlight, but not on boiling, or storing in the dark. A continuation of this work shows that it is only the unsaturated compounds diamidino-stilbene (R.CH : CH.R, when

R is an amidino-benzene group), its mono methyl derivative (R.CH. (CH_3) : CH.R), and diamidino-tolane (R.C. : C.R) which are affected in this way. Saturated compounds such as diamidino-diphenoxy-pentane (pentamidine, R.O. $(CH_2)_5$.O.R) or diamidino-diphenyl-ethane (R.CH_2.CH_2.R) were not affected, nor was diamidino-dimethyl stilbene (R.CH.$(CH)_3$.CH (CH_3).R). With stilbamidine the change occurred rapidly and it could be demonstrated after exposure of half an hour to winter sunlight. According to Fulton's findings, and to those of BARBER, SLACK & WIEN [this *Bulletin*, 1943, Vol. 40, p. 376] water is added on at the unsaturated linkage according to the equation :—

R.CH : CH.R + H_2O → R.CHOH. CH_2.R (diamidino-phenyl-benzyl-carbinol)

As a result of these changes, the solutions became much more toxic for mice while the therapeutic activity is somewhat diminished. Some of the solutions also became yellow. The practical significance of these findings is, that solutions of the unsaturated amidines should be stored away from light, or, better still, that they should be freshly prepared before use. *F. Hawking.*

GOODWIN (T. W.). **The Spectroscopic Examination of certain Aromatic Diamidines before and after Exposure to Light.**—*Ann. Trop. Med. & Parasit.* 1943. Apr. 30. Vol. 37. No. 1. pp. 59–65. With 6 figs.

Using spectroscopic methods, Goodwin confirms the findings of FULTON (above) that stilbamidine and similar unsaturated compounds undergo photochemical alteration when exposed to light. *F. Hawking.*

KIRK (R.) & SATI (Mohammed Hamad). **Further Notes on some Cases of Sudan Kala-Azar treated with certain Aromatic Diamidines.**—*Ann. Trop. Med. & Parasit.* 1943. Apr. 30. Vol. 37. No. 1. pp. 34–37.

In previous papers [this *Bulletin*, 1941, Vol. 38, pp. 261 and 573] the authors reported that during the latter half of 1939 and the first half of 1940 they had treated a number of cases of kala azar in the Sudan with certain aromatic diamidines. The present report deals with 44 cases, of which 43 were treated by the authors. There were eight deaths, giving a case mortality rate of 18 per cent. Of the eight patients who died, five were admitted to hospital in an extremely advanced stage of illness and died after a few injections ; another died after a debauch. The remaining 36 were discharged from hospital as provisional cures. In all these cases the drug was administered in a solution which was freshly prepared immediately before each injection. Subsequent observations have shown that this is a factor of paramount importance in the avoidance of toxic effects. The present report describes the follow-up of these cases after a period of two and a half to three years. Of the 36 patients it was not possible to trace four, while three are known to have died. Of the untraced persons two were known to be alive and well 3 and 5½ months after discharge. The three deaths occurred 6, 18 and 22 months after discharge. These results of treatment and the drugs employed are given in the following table :—

TABLE.—*Showing the final results of treatment in* 43 *cases of Sudan kala-azar treated with three aromatic diamidines.*

	4 : 4′-Diamidino stilbene	4 : 4′-Diamidino diphenoxy propane	4 : 4′-Diamidino diphenoxy pentane	Total
Admitted to hospital ...	28	2	13	43
Died in hospital	4	1	3	8
Discharged, provisional cure	24	1	10	35
Died subsequently ...	1	0	2	3
Known to be alive and in good health 2½ years later	20	1	7	28
Could not be traced 2½ years later	3*	0	1†	4

* One case was seen and appeared well 5½ months after discharge as provisionally cured.

† Was seen and appeared well 3 months after discharge as provisionally cured.

C. M. Wenyon.

SENEKJI (Harry A.). **Hematologic and Immunologic Studies on Natural and Induced Leishmaniasis in Paretics.**—*Amer. Jl. Trop. Med.* 1943. Jan. Vol. 23. No. 1. pp. 53–58.

The author has made studies of blood in 22 cases of cutaneous leishmaniasis. There were no changes from the normal in any of the cases and in every instance the formol gel test was negative. In the case of four general paralytics who had previously had cutaneous leishmaniasis, intravenous injections of from 9 to 100 million leptomonads from cultures of *Leishmania tropica* were made. All four developed fever (40°C.) of three days' duration. One subject, without any previous history of leishmaniasis, developed, in addition to the fever, hepato- and spleno-megaly and obstructive jaundice which lasted for 10 days. In all five cases there was improvement in the mental condition. Two patients, immune to *L. tropica*, were injected with large doses of culture of *L. donovani*, but kala azar did not develop. Similarly no infection followed the injection of *L. brasiliensis* in a case with a previous history of oriental sore. It is suggested that injection of cultures of *L. tropica* is a promising line of treatment for general paralysis.

C. M. Wenyon.

FEVERS OF THE TYPHUS GROUP.

PLOTZ (Harry), SMADEL (Joseph E.), ANDERSON (Thomas F.) & CHAMBERS (Leslie A.). **Morphological Structure of Rickettsiae.**—*Jl. Experim. Med.* 1943. Apr. 1. Vol. 77. No. 4. pp. 355–358. With 7 figs. on 2 plates. [10 refs.]

Rickettsiae of "epidemic typhus," "endemic typhus," Rocky Mountain spotted fever, and Q fever, have been examined with th

help of the electron microscope (type B R C A). The organisms were obtained from yolk-sac cultures and were spread on collodion films. Details of the technique will be given in another paper.

The Rickettsiae of all the four diseases were strikingly similar to each other in appearance. The bacillary forms are seen to have a limiting membrane enclosing a substance which is moderately opaque to electrons ; in these respects they resemble bacteria. Like certain kinds of bacteria they contain granules in the protoplasm. The smaller coccoidal forms, which cannot be distinguished with certainty from tissue particles by ordinary methods, are found to have the same structural appearance as the bacillary forms ; their outline is oval. They may represent the " Invisible Rickettsiae " whose presence has been postulated to explain the infectivity of material in which no Rickettsiae can be seen in stained films.

Great variations occur in the morphology of the Rickettsiae of each of the four species, but the basic structure is the same in all, and it has not yet been found possible to distinguish the different species by their appearance.

The structure of viruses as seen by the electron microscope does not show these variations in appearance, but is relatively uniform. The elementary bodies of vaccinia virus are brick-like in shape and most of them have five symmetrically arranged internal granules.

The paper is illustrated by two plates, one of which shows photomicrographs of stained smears containing Rickettsiae at a magnification of 1,000 diameters ; the other shows electron micrographs of the four species of Rickettsiae investigated, at a magnification of 16,000 diameters.

[This description of the morphology of various Rickettsiae as revealed by the electron microscope is of great interest. It seems to confirm the view that Rickettsiae occupy a position intermediate between bacteria and filterable viruses, and it lends support to the view that the Rickettsiae of the various fevers of the typhus group are closely related to each other.] *John W. D. Megaw.*

ROBINSON (P.). **Typhus Fever in Addis Ababa.**—*Ann. Trop. Med. & Parasit.* 1943. Apr. 30. Vol. 37. No. 1. pp. 38–41. [13 refs.]

This note is based on 400 cases of louse-borne typhus observed between May 1941 and January 1942. Tick-borne and mite-borne forms of typhus are not known in Addis Ababa. *Proteus OXK* agglutinins have been found by the author to occur in high titres in all cases of relapsing fever.

Early diagnosis of typhus was not easy because the rash could be detected in only 6 per cent. of the cases. Albuminuria was an almost constant feature and the blood pressure was low, averaging 60 to 80. Malaria and relapsing fever coexisted in 18 and 8·5 per cent. respectively of the cases. The Weil-Felix reaction was very reliable but did not become positive till the 15th day or later in about half of the cases. Weigl's vaccine, prepared locally by pupils of Weigl, was found useful in early diagnosis ; doses of 1 to 10 millions of Rickettsiae caused a powerful local reaction in healthy persons but in 54 cases of typhus there was no reaction, even at early stages while the Weil-Felix response was still negative. In 70 other cases in which the Weil-Felix was positive there was no reaction. [No mention is made of the days

of the disease on which the absence of reaction was observed, and more information about this interesting observation would be welcome.]

In a few cases, after 7 to 10 days of apyrexia, there was a second spell of fever during which four patients developed fatal pneumonia. Some children had no symptoms of any kind except fever lasting one or two days. In one fatal case there was no history of fever but only severe oedema of both legs; the diagnosis was made on the strength of a strongly positive Weil-Felix reaction and the findings at the autopsy.

In treatment novasurol was useless, sedatives were preferred. Strophanthin was of value in acute heart failure. Unconscious patients were given one-half to one litre of isotonic glucose.

There was reason to believe that some of the patients had suffered from previous attacks. The mortality rate was 6 per cent. Weigl's vaccine was used with success for the protection of the medical staff.

John W. D. Megaw.

ALWENS (Walter). Klinik des Fleckfiebers. (Frankfurt a.M., Medizinische Gesellschaft, 30.VI.1942.) [**Clinical Aspects of Typhus Fever.**]—*Deut. Med. Woch.* 1943. Mar. 12. Vol. 69. No. 10. pp. 239–240.

This is a report of an address given at a meeting of the Medical Society of Frankfurt-on-Maine in June 1942. It contains little that is new but is of interest as a summary of the experiences of German medical workers in the winter of 1941–42.

The account of the symptoms is on the usual lines, but it is stated that absence of the rash is by no means always associated with short or mild attacks. Apart from the manifestations due to the formation of nodules in the blood vessels, toxins play an important part in causing early disturbances of the nervous system, and convalescent serum given twice daily is often helpful in combating these. Loss of hair from the back of the head and parts of the legs was of frequent occurrence. Apart from low blood pressure there may be various special lesions of the cardiac muscle and nerves, which can be detected by the electrocardiograph. The practical value of the Weil-Felix reaction is undoubted, in spite of occasional failures. A positive Wassermann reaction may occur up to the sixth week; in the author's experience this happened in 13 per cent. of the cases.

Protective inoculation is of great value; this is shown by the mildness of the attacks in persons of 50 years and over, who, apart from inoculation, would have little chance of survival.

The author, like most German physicians, is a firm believer in the value of cardiac tonics; he advocates intravenous injections of strophanthin in doses up to one milligramme daily. Intravenous transfusions of glucose or normal saline solutions are recommended; these are given twice daily. Among the numerous drugs mentioned with approval are camphor and caffeine. Sulphonamides are said to be useless except in preventing bronchopneumonia. Cold-bath treatment as for typhoid fever is useful when the temperature is high. For circulatory collapse the hot-bath treatment recommended by LAMPERT is advised. Vitamins B and C should be given. Open-air treatment is of value when practicable. In the early stages doses of 100 cc. of convalescent serum, repeated when required, are said to shorten the

febrile period and improve the general condition of the patients. The author advocates the establishment of an organized system for collection of convalescent serum. *John W. D. Megaw.*

SÜPFLE (K.) & FISCHER (H.). Erfahrungen ueber die Weil-Felix-Reaktion. [**Experiences with the Weil-Felix Reaction.**]—*Arch. f. Hyg. u. Bakt.* 1943. Vol. 129. No. 1/6. pp. 158–166.

The observations deal with cases of typhus of average severity (mortality rate of less than 10 per cent.).

The bacterial suspensions were made mostly from the "dry diagnostic strain (Cracow)" which was very satisfactory and convenient.

Contrary to the usual statements the authors found that reactions which appeared late often rose to high titres; in one case a reaction which became positive after the 30th day rose to a titre of 1–12,800 thirteen days later. The highest titre was reached before the end of the fever in 59 per cent., on the last day of the fever in 11·4 per cent., and after the end of the fever in 29·6 per cent. of the cases.

Leaving out of account titres below 1–200, 76 per cent. of the cases had titres rising to maxima of 1–1,600 to 1–6,400; only 2·3 per cent. were as low as 1–200, and 5 per cent. reached 1–25,600.

Usually the titre fell to 1–50 or less four to six weeks after the onset, though occasionally titres of 1–3,200 or more were observed eight to nine weeks after the onset.

No association was found between the severity of the attacks and the height or rapidity of rise of the titre.

Negative reactions and weak positives of 1–50 or under were seen in only 0·8 per cent. Reactions of 1–100 are suggestive of typhus, but even those of 1–200 are not absolutely diagnostic. Titres of 1–400 were never seen in diseases other than typhus.

Rickettsial agglutinations were positive in several cases in which the Weil-Felix reaction was negative or weakly positive: one patient whose Weil-Felix was negative had a positive Rickettsial reaction of 1–12,600, and three whose Weil-Felix titre was 1–50 reacted to Rickettsiae at 1–160.

In trench fever the Weil-Felix reaction was sometimes weakly or moderately positive; in two cases the titre was 1–50, in five, 1–100, and in one, 1–400; in the last the Rickettsial titre was 1–160. Positive reactions were observed in ten cases which were not typhus; in nine of these the titre was 1–100, in the other, 1–200.

In half of the cases of typhus the titre rose to 1–400 or over between the third and eighth days, and often the reaction gave the first indication of the correct diagnosis.

Dealing only with cases in which the titre was 1–400 or over, this titre was reached on the third day in 4·5 per cent., on the fourth day in 5·5 per cent., on the fifth day in 5·5 per cent., on the sixth day in 13 per cent., on the seventh day in 15 per cent., on the eighth day in 14 per cent.; from the ninth to the thirteenth day in 43 per cent.

The reaction was tested in a group of persons recently inoculated with an unspecified vaccine against typhus fever; about half of these had positive Weil-Felix reactions in titres of 1–50 to 1–200 a fortnight or three weeks after inoculation, but the reaction soon became negative.

A number of cases of typhus had been wrongly diagnosed as typhoid on the strength of Widal reactions in titres which were sometimes as

high as 1–800 or over ; these were all in persons who had been inoculated against typhoid fever.

Patients who were attacked with typhus after anti-typhus inoculation usually reacted to the Weil-Felix test in lower titres than uninoculated patients. *John W. D. Megaw.*

WARNECKE (Bernd). Unspezifische Luesreaktionen bei Fleckfieber. [**Non-Specific Luetic Reactions in Typhus Fever.**]—*Arch. f. Hyg. u. Bakt.* 1943. Vol. 129. No. 1/6. pp. 167–173.

Reports of the occurrence of Wassermann reactions in typhus fever are scanty and conflicting. Some of them are of little value because the sera had not been inactivated before being tested.

The authors carried out the Wassermann, Kahn, and Meinicke (MKR II) tests, at intervals of four days during the febrile and convalescent periods in an unspecified number of cases of typhus fever.

The reactions to all three tests were negative in 83·4 per cent. and positive to one or more of them in 16·6 per cent. The reactions were never positive before the ninth day and were most frequently observed shortly before the end of the fever or early in convalescence, and remained positive only for a short time. The results with the three tests were inconsistent ; it was exceptional to get positive reactions to all three tests at the same time ; the Kahn reaction was more often positive than the other two.

Delayed non-specific reactions were sometimes observed ; the most extreme cases of these were a reaction to the Kahn test between the 11th and 45th days of convalescence and one to the Meinicke test between the 39th and 51st days. The reactions on the whole were either weakly or moderately positive, and persistent luetic reactions occurred only in cases of known or strongly-suspected syphilis.

Healthy persons who had been inoculated with Weigl's vaccine never gave positive reactions to any of the tests.

The pallida reaction of Gaehtgens was negative in all the cases in which it was carried out. *John W. D. Megaw.*

MEYER (Richard). Ueber das Verhalten von Citochol- und Meinicke-Klärungsreaktion beim Fleckfieber. [**The Citochol and Meinicke Reactions in Typhus Fever.**]—*Ztschr. f. Immunitätsf. u. Experim. Therap.* 1943. Feb. 12. Vol. 102. No. 6. pp. 459–466.

These tests were made on 712 samples of sera in which the Weil-Felix titres were 1–100 and over. Doubtful (+ to ++) and definitely positive (+++ to ++++) reactions occurred in 26·3 per cent. of the cases with the Citochol test, and in 10·5 per cent. with the Meinicke test. Simultaneous reactions to both tests occurred in only 4·5 per cent. of the cases, and the reactions were never definitely positive to both tests at the same time. Taking into account only the definitely positive reactions, these occurred to one or other of the tests in 2·0 per cent. of the cases, and only for short periods of time.

There was no association between the occurrence or strength of the reactions and the titres of the Weil-Felix responses ; negative, doubtful, and definitely positive reactions, were about equally distributed between cases with low and those with high Weil-Felix titres.

The patients were kept under observation for four weeks only ; positive reactions were found to occur in some cases up to the end

of this period. In soldiers who had been living for long periods in areas of typhus endemicity doubtful reactions were proportionally much more frequent than in those who had recently come from Germany, but factors other than typhus fever may be concerned. For example, two cases of malaria were wrongly diagnosed as typhus fever: in one of these the Weil Felix titre was 1–100 and there was a doubtful (+) Meinicke reaction; in the other the Weil-Felix titre was 1–200, the citochol reaction was strongly positive (++++) and the Meinicke reaction doubtful (++). *John W. D. Megaw.*

TOPPING (Norman H.) & DYER (R. E.). **Apparent Recent Extension of Typhus in the United States.**—*Amer. Jl. Trop. Med.* 1943. Jan. Vol. 23. No. 1. pp. 37–42. [18 refs.]

The geographical distribution of "endemic" typhus [flea-borne] in the U.S.A. is discussed with reference to reports received up to January 1942. Georgia is the chief area of endemicity, with about 1,000 cases yearly: Alabama, Mississippi, South Carolina, Louisiana, and Texas, taken together have about the same number. Cases are also reported every year from Boston, New York, Baltimore, Norfolk, Wilmington, Charleston, and Savannah; all on the east coast. Recently cases have occurred in Tennessee and California. The disease is mostly urban but increasing numbers of cases are being reported from rural areas in the south-eastern States. Although the disease appears to be spreading it is still confined in the main to the south-eastern and southern States.

The authors now report isolated cases from Richmond, Washington, St. Louis, Cincinnati, and Cleveland: these are regarded as being well authenticated, though the isolation of Rickettsiae from rat fleas in the neighbourhood has been carried out in only one of the cases. The patient from St. Louis was a Russian who had immigrated 36 years previously, and it is stated that four cases of suspected typhus reported from that city in 1924 were also in Russians, and that no further cases had been reported till the one now described. [The possibility that these may have been cases of Brill's disease is not discussed.]

The tropical rat flea, *Xenopsylla cheopis*, has been found on rats in Iowa and several other mid-western States. Physicians are advised to be on the look-out for the disease because it may be more widely distributed than is at present suspected. *John W. D. Megaw.*

BRIGHAM (George D.) & PICKENS (Edgar G.). **A Strain of Endemic Typhus Fever Virus isolated from House Mice** (*Mus musculus musculus*).—*Public Health Rep.* 1943. Jan. 22. Vol. 58. No. 4. pp. 135–136.

SCHEINKER (I. Mark). **Histologic Observations on the Changes in the Brain in Rocky Mountain Spotted Fever.**—*Arch. Pathology.* 1943. Apr. Vol. 35. No. 4. pp. 583–589. With 2 figs. [14 refs.]

A woman, aged 67 years, died 10 days after the onset of a fever in which there was a generalized macular haemorrhagic rash affecting the whole of the body except the face. The patient and two children were attacked by fever about a fortnight after returning from a visit to Kentucky. No mention is made of a bite by a tick and the description of the agglutination reaction is in the words "The Weil-Felix reaction in the blood was positive."

Rickettsial bacteriaemia was found in the skin, liver, kidneys, and the spleen, in the autopsy. Histological examination of the brain showed endothelial proliferation, which was irregularly diffused, and accompanied with changes in the medullary vessels. The granulomata consisted of "nodules" accumulations of large irregular polygonal or fusiform mononuclear cells of varying size. The nodules showed cells with degeneration. In the brain a cell granuloma there was actually a medullary vessel with proliferation that showed no inflammation. The cell elements appeared to have been formed from the adventitial cells of the capillary. These cells had proliferated and included the surrounding nerve structures.

The final stage in the process was the necrosis of the cells and the disintegration of the capillaries. There was also representation of the perivascular cells in the immediate neighbourhood of the granulomata, and a slight degree of infiltration in the neighbouring cells.

The condition was regarded as an hyperplastic vasculitis of the adventitial nerve cells, a measurable proliferation.

Good photomicrographs illustrate the article.

No doubts are expressed about the accuracy of the diagnosis. Though the evidence on which it was based is not fully stated. The description of the lesions agrees fairly closely with that of Dawson, who was dealing with the two cases of cerebro-spinal fever, although that Dawson dealt by special pathologists rather than the pathologists as being effective for his benefit. [illegible]

[illegible] F. P. Wright.

Spencer, Edward A. & Parker, R. R. **Experimental Rocky Mountain Spotted Fever. Results of Treatment with certain Drugs.** [illegible] Vol. 38, No. 8, pp. 85–382.

The authors have used sulphathiazole, sodium sulphathiazole, sulphapyridine, sulphanilamide, and prontosil on the treatment of guinea-pigs inoculated with the virus of Rocky Mountain spotted fever Rickettsia. No effects of therapeutic value could be discovered in any of these drugs in spite of the varied dosages employed.

[illegible]

Parker, R. R. & Spencer, Edward A. **Rocky Mountain Spotted Fever. Duration of Potency of Tick-Tissue Vaccine.**—[illegible] Vol. 38, No. 8, pp. 380–382.

Ticks were counted during these summers on the Spencer-Parker farm in Rocky Mountain spotted fever vaccine prepared from the tissues of infected ticks. These had been stored for 12 to 14 years at a temperature range of 36° to 40°F. and all these were found to have retained their infectivity.

The ticks were of the standard type through used for many years and [illegible]. Six guinea-pigs were used for each sample, each was injected [illegible] and 12 days later was inoculated by the intraperitoneal route with 1/40 c.c. infected heart-blood taken on the third day of fever from a guinea-pig infected with a virulent strain of Rocky Mountain fever; this last, on the average, represents 500 infecting doses. The resulting protection was [illegible]

at least equal to that obtained 12 to 14 years previously with the same lots of vaccine. Only three of the 18 guineapigs used gave febrile reactions and these lasted only for a day or two.

John W. D. Megaw.

WESTPHAL (Karl). Ueber eine eigenartige fieberhafte Erkrankung in der Ukraine. [**A Peculiar Fever in Ukraine.**]—*Deut. Med. Woch.* 1943. Feb. 5. Vol. 69. No. 5. pp. 97–100. With 3 figs.

Many cases of a "problem" fever were seen in Eastern Ukraine from January to July [? 1942]. The onset was like that of mild typhus, with chill and severe headache, but without pronounced psychic disturbance. Pains in the limbs and back were not severe. The spleen was enlarged in 80 per cent. of the cases. There was relative bradycardia. A rash was seen in 70 per cent. of the cases "at the beginning of the fever." It was macular, very slightly papular, and was chiefly on the upper part of the trunk, sometimes extending to the arms, never to the face. It lasted only one or two days as a rule; exceptionally it persisted for three or four days. The fever was continued, with morning remissions, and the temperature fell gradually towards the end of the attack, which lasted usually for six to ten days, but occasionally for three to five only.

There was no leucocytosis; the tendency was rather towards leucopenia. The diazo reaction was positive. Asthenia persisted for two or three weeks after the end of the attack.

Five doctors and three sanitary officers were attacked, but there were no special epidemiological conditions; lice, fleas, bugs, and rats, were not specially plentiful. The affected troops had been living in primitive Russian huts. The disease was widespread in the Ukraine and the name "Ukrainian fever" is suggested.

The Weil-Felix reaction, tested on two to four occasions in each case, was often negative, but more often was positive in titres of 1–50 to 1–100, seldom of 1–200, and never in higher titres. In one case an attack of verified typhus occurred about a month after recovery from the fever. The Widal reaction was negative or weakly positive, and blood cultures were negative.

The fever differed from the recognized types of trench fever in the absence of shin-bone pains, in the occurrence of splenic enlargement together with a rash at the onset, and in the absence of prolonged attacks. The seasonal distribution also did not correspond with that of trench fever, which was common in the affected region. The possibility of its being a hitherto unrecognized type of trench fever is not excluded.

[The reviewer is inclined to think that the disease may turn out to be caused by Rickettsiae of the trench-fever type. Trench fever is a protean disease and may be a group of fevers rather than a single clinical entity.]

John W. D. Megaw.

YELLOW FEVER.

HARGETT (M. V.), BURRUSS (H. W.) & DONOVAN (Anthony). **Aqueous-Base Yellow Fever Vaccine.**—*Public Health Rep.* 1943. Mar. 26. Vol. 58. No. 13. pp. 505–512. [28 refs.]

Since 1936 a number of reports have been published on immunization against yellow fever by 17D vaccine prepared from an extract of infected

chick embryos in non-immune human serum [see this *Bulletin*, 1937, Vol. 34, p. 691; 1939, Vol. 36, p. 648; 1941, Vol. 38, p. 70]. After a considerable experience with this vaccine it became evident that the use of human serum as a component of the vaccine gave rise to a definite risk of delayed hepatitis. The Laboratory of the Yellow Fever Service in Brazil therefore began, in December 1940, to eliminate human serum completely in the preparation of the vaccine, using the infected chick embryo extract alone [see this *Bulletin*, 1943, Vol. 40, pp. 41–44]. The "serum-base" vaccine continued to be generally employed, while studies on the "aqueous-base" product were under way.

The United States Public Health Service began the production of yellow fever vaccine in its Rocky Mountain Laboratory at Hamilton, Montana, in February 1941. A field study on the comparative behaviour of serum-base and aqueous-base 17D vaccine was then undertaken at Oroya, Peru, and in Montana on small groups of people. The results of these studies showed both types of vaccine to be equally effective. The outbreak of jaundice among American troops following the use of serum-base vaccine precipitated a demand for serum-free vaccine, so the large-scale production of aqueous-base vaccine was started early in 1942 and, at the time this report was written, over 600,000 doses had been released for human use.

The fundamental techniques for the preparation of the aqueous-base vaccine are the same as previously described [see this *Bulletin*, 1939, Vol. 36, pp. 648–649]. The details of the method now recommended by the authors are as follows: Fertile hen's eggs are incubated, as for hatching, for seven days. Those eggs showing viable embryos are then each inoculated with 0·05 ml. of 227th–230th passage 17D virus, *via* a small hole drilled through the shell. Egg passage, rather than tissue-culture propagated, virus is employed. After sealing the inoculation holes with hot wax, the eggs are returned to incubation as before for a further 90–96 hours. The eggs are then opened and the living embryos are triturated in a homogenizer. For each three grammes of embryo there is added 1·0 ml. of distilled water. The finely divided tissue extract is centrifuged for 30 minutes at 3,500 r.p.m. and the supernatant liquid is drawn off. Specimens are taken for sterility tests and for determination of virus concentration in mice; the remainder of the extract is put into a one-litre pyrex bottle and frozen in a thin shell by rotating in an alcohol-dry ice mixture. The frozen extract is then kept at minus 60° to minus 78°C. pending the results of the sterility and virus tests. If the tests are satisfactory, the extracts are melted and distributed in quantities of 1·0 and 5·0 ml. into ampoules.

The ampoules of vaccine are then dried under vacuum from the frozen state, employing a "lyophile" type desiccator. The desiccation process lasts 21 hours. The desiccation system is then filled with dry nitrogen and the ampoules promptly sealed. The ampoules are labelled, packed in boxes, and stored at a temperature of minus 16° to minus 30°C. Refrigeration during shipment is maintained by packing the vaccine in carbon dioxide ice in a glass vacuum flask. It is recommended that the vaccine be kept at a below-freezing temperature until actual time of use. On removal from refrigeration, it is rehydrated to original volume with physiological salt solution and is then diluted 1 : 10 with additional saline. Each recipient is given 0·5 ml. subcutaneously. The vaccine must be used within one hour following

rehydration. No unfavourable reactions have been reported among the large series of people who have received vaccine prepared by the authors.

To be accepted for human use a batch of vaccine must conform to the following requirements :—

1. Sterility cultures must show no growth.
2. None of a series of three guineapigs inoculated intraperitoneally may show illness or a temperature of more than 39·7°C. during the two weeks immediately following injection.
3. A minimum of 66,000 minimum lethal mouse doses of virus per millilitre must be present.
4. The test monkey inoculated intracerebrally must show circulating virus and a reversal of protection test ; *i.e.* the preinoculation serum specimen must show virus-neutralizing bodies absent, and the post-vaccination specimen show them present. The animal must recover from any illness incurred, without signs of paralysis having developed at any time. The vaccine is discarded if the test monkey develops paralysis or dies, regardless of apparent cause. *Hugh H. Smith.*

LAEMMERT (H. W.), Jr. **Studies on Susceptibility of certain Poikilothermal Animals to Yellow Fever Virus.**—*Amer. Jl. Trop. Med.* 1943. Mar. Vol. 23. No. 2. pp. 227–235.

In the course of investigations on yellow fever in the Villavicencio area of Colombia and the region around Rio de Janeiro, Brazil, various poikilothermal animals were collected and tested in the laboratory for their susceptibility to yellow fever virus. Among the animals studied were iguanas, lizards, tortoises, boas, toads, and frogs. The virus was inoculated by various routes and in varying dosages. The Asibi, French, and four South American strains of virus were employed in the tests. Blood sera of the larger species were tested for the presence of virus on successive days after inoculation ; the sera were injected intracerebrally into mice. The smaller animals were sacrified one each day ; the liver was removed aseptically and suspensions made for intracerebral inoculation into mice. To determine whether the animal was capable of responding to the test dose by producing antibodies, serum specimens were obtained for the mouse protection test at intervals after the inoculation.

The author concludes that no unequivocal evidence was obtained that yellow fever virus is capable of multiplication in the animals tested. In general the animals showed a very poor antibody response after inoculation with large doses of the virus. *Hugh H. Smith.*

DENGUE AND SANDFLY FEVER.

HALLMANN. Beitrag zum Pappatacifieber 1941 auf der Balkanhalbinsel. [**Sandfly Fever in the Balkan Peninsula in 1941.**]—*Deut. Trop. Ztschr.* 1943. Feb. 1. Vol. 47. No. 3. pp. 64–68. With 6 charts.

An outbreak of a mild type of sandfly fever occurred among the troops stationed in the islands and mainland of the Athens region. It lasted from June to September, but most of the cases were seen in July and

August ; in these two months 20 per cent. of the troops in the area were attacked. Other cases must have occurred in men stationed in outlying posts. The report deals with 86 cases treated in hospital.

In 93 per cent. of the cases the fever lasted two or three days, in the rest it lasted four or five days.

The axillary temperature seldom exceeded 38° to 39°C. ; in three cases it was more than 40°C. There was conjunctival injection in 35 per cent. of the patients ; the face was flushed. Gastro-intestinal disturbances occurred in 10 per cent. during the febrile period. In 82 per cent. there was headache, localized in the orbital, frontal, and temporal regions. There was no pronounced bradycardia. There were no complications, but neuralgic pains sometimes persisted for a few days after the fall of the temperature.

Malaria, dysentery, and influenza were the conditions calling for differential diagnosis ; stress is laid on the need for examining thick blood films to exclude malaria.

Aspirin, in daily doses of 1·5 to 3 grammes, was given to most of the patients ; this had no effect on the duration of the fever but gave relief to the pains. The period of incapacitation for duty was only four or five days. *John W. D. Megaw.*

PLAGUE.

Douglas (J. R.) & Wheeler (C. M.). **Sylvatic Plague Studies. II. The Fate of *Pasteurella pestis* in the Flea.**—*Jl. Infect. Dis.* 1943. Jan.–Feb. Vol. 72. No. 1. pp. 18–30. With 14 figs. & 1 chart. [12 refs.]

Detailed work of a strict laboratory type is being carried on by the authors and this article is packed with information of practical importance. Two fleas have been used in comparative experiments, one the accredited chief vector of human plague, the rat flea *Xenopsylla cheopis*, and the other the test flea, common on California ground squirrels, *Diamanus montanus*. A very full account of methods is given ; the number of fleas used is considerable and photomicrographs of sections of infected and non-infected fleas add much to the interest of the investigation. This research once more emphasizes " that the transmission of *Past. pestis* by fleas is absolutely dependent on the multiplication of the bacilli in the alimentary tract of the insect." It has not been confirmed, however, that the faecal droplets of infected fleas consistently contain large numbers of plague bacilli. Indeed this shedding of bacilli is so irregular that it seems unlikely that faecal matter of the flea is much concerned in the infection of the mammalian host.

In this research white mice were used. It only required an intraperitoneal inoculation in mice of some 20,000 plague bacilli to give rise to a maximal bacteraemia (10 million per cmm. of blood) within 48 hours. By the method of the authors for calculating the capacity of the stomach of *Diamanus montanus* and *X. cheopis*, " from the number of organisms ingested in the blood meal," a figure (0·03 cmm.) was obtained, which is much smaller than the average (0·5 cmm.) of the Indian Plague Commission.

Comparing the two fleas they found that the oesophagus of *D. montanus* is " invaded twice as frequently as that of *X. cheopis* " and that blocking of the alimentary tract required 16 days in the former to 10 days in the latter. The ability of the fleas to free their alimentary canal of plague bacilli after a single blood meal differed also in the two cases ; approximately 60 per cent. of infected *D. montanus* and only 2 per cent. of *X. cheopis* are able to do so. This may occur in 24 hours in *D. montanus* and take more than 48 hours in *X. cheopis*. It must not be assumed, however, from these data alone that *X. cheopis* is a better vector of plague than *D. montanus*. The vector efficiency cannot be judged in this way only ; " the percentage of fleas which become infective and the number of transmissions effected by them must be taken into consideration," as well as other factors.

W. F. Harvey.

EVANS (F. C.), WHEELER (C. M.) & DOUGLAS (J. R.). **Sylvatic Plague Studies. III. An Epizootic of Plague among Ground Squirrels** (*Citellus beecheyi*) **in Kern County, California.**—*Jl. Infect. Dis.* 1943. Jan.-Feb. Vol. 72. No. 1. pp. 68–76. With 1 fig. [17 refs.]

That plague may exist in a district or country long before it has been demonstrated is now a well-known fact. Plague was only proved to exist in Kern County in 1934 " when it was isolated from ground squirrels, but older residents of the county recall occasions dating from the early years of this century when these squirrels died in large numbers." Surveys were, however, made of Kern County in 1908, 1910, 1911, 1916, 1932 and 1933, " but no plague was discovered." In March 1934 report came that squirrels were dying in the same area as reported in the previous year ; a survey now gave positive results. Of 3,416 squirrels examined 118 yielded cultures of *P. pestis*. Since 1934 " surveys and control measures have been carried on every year ;" the surveys were uniformly negative until 1941. There have been no human cases in Kern County. In 1941 the presence of plague was reported in five localities and the authors' findings in this epizootic are summarized :—Previous outbreaks indicate that plague is enzootic in Kern County. " There was no evidence of infection among the squirrels during the breeding season. The epizootic ran a separate course in each area and coincided fairly well with the period of dispersal of the young squirrels. . . . An inapparent infection was demonstrated in young squirrels at the end of October ; this may represent a true latent infection . . . Fleas apparently provide at least a temporary shelter for the plague bacilli when the rodent host population is low." The burrows may perhaps be regarded as centres of infection. Here fleas " have been known to survive as long as 63 days after experimental infection." Plague infection was demonstrated in the fleas *Diamanus montanus*, *Hoplopsyllus anomalus* and *Echidnophaga gallinacea*.

W. F. Harvey.

AMOEBIASIS AND INTESTINAL PROTOZOAL INFECTIONS.

D'ANTONI (Joseph S.). **Further Observations on Amebic and Bacillary Colitis in the New Orleans Area.**—*Amer. Jl. Trop. Med.* 1943. Mar. Vol. 23. No. 2. pp. 237–242.

This is a contribution on much the same lines as the one recently reviewed in this *Bulletin*, 1943, Vol. 40, p. 53.

The present study deals with patients observed since April 1941 and who were investigated for chronic colonic symptoms; 236 patients were seen and fell into two groups. Subjects in the first group were available for thorough examination and could be followed up for prolonged periods. Investigation consisted of microscopic examination of three normally passed stools over a period of one week, as well as of specimens passed after taking a purgative or an enema, and sigmoidoscopic examinations. During the latter, material from suspected areas was aspirated, examined and cultured for dysenteric organisms. In the second group were included hospitalized patients referred to the Department of Tropical Medicine for sigmoidoscopy. No faecal specimens were, therefore, examined prior to sigmoidoscopy. The purgative consisted of sodium sulphate, and the follow-up continued for limited periods only. Part of the aspirated material was cultured for dysentery bacilli.

There were 36 patients positive for *Entamoeba histolytica*. The lesions were classified as one plus, or two plus, depending on whether fewer or more than thirty typical pinpoint amoebic lesions with characteristic exudate and normal intervening mucosa were present. It became obvious from 12 cases with absence of rectal lesions that caecal amoebiasis can rarely be diagnosed by examination of aspirated material; it therefore depends on recovery of the organism from normally passed or purgation stools.

In one group of 173 patients, in whom one stool examination was performed, 39 harboured *E. histolytica*, an incidence of 22 per cent. This group represented individuals in whom a low grade and mildly debilitating infection was predominant. In three, tumours or "amoebomata," which disappeared after anti-amoebic therapy, were demonstrated.

In 7 per cent. mixed infections with Shiga organisms were detected.

Five strictures typical of lymphogranuloma inguinale were found to coexist, and there was a case of sprue with superadded amoebiasis.

The term "Shigella colitis" is suggested for cases in which the colitis syndrome is associated with Shigella organisms. The bowel showed a dark red, granular appearance with secondary infection, regarded by many as an early stage of non-specific colitis.

Other diseases were revealed, such as carcinoma and undulant fever. Within the past few years it has become apparent that both *Brucella melitensis* and *Br. abortus* may produce a colitis.

Thirty-four cases of non-dysenteric amoebiasis and 12 of amoebic dysentery have been treated with Diodoquin (Searle). The course of treatment was three tablets (3·2 grains) three times daily to adults for 20 days. Four children (aged 6–11) received two-thirds of this dosage. A minimum of three negative stool specimens at least two weeks after completion of treatment, and whenever possible spread over a period of one week, was taken as a criterion of cure.

Examination included the direct faecal film and the zinc concentration technique. In 44 out of 46 cases the drug caused the disappearance of *E. histolytica*. The drug failed in two cases, but in one was later successful. *P. Manson-Bahr.*

SIEYRO (Luis). Die Hausfliege (*Musca domestica*) als Ueberträger von *Entamoeba histolytica* und anderen Darmprotozoen. [**The House-Fly as Carrier of** *E. histolytica* **and other Intestinal Protozoa.**]—*Deut. Trop. Ztschr.* 1942. July 15. Vol. 46. No. 14. pp. 361–372.

The carriage of intestinal protozoa by house flies has been the subject of investigation by a number of observers since WENYON and O'CONNOR first showed in 1917 that flies feeding on faecal material ingested the protozoa and subsequently passed them unaltered in their faeces. It was evident that flies were capable of depositing their faeces on material destined for human consumption and this passage of the protozoa, particularly the cysts, through the intestine of the flies in as short a time as five minutes afforded better opportunities of transmission than the possible adherence of infected material to the feet or proboscis, where rapid drying would occur. The viability of the cysts escaping from the flies' intestine was based on the eosin test, in which it was assumed that cysts staining with eosin were dead and those not so staining were alive. In the case of trichomonas such a test was not necessary, for it was shown that the flagellates passed by the flies were still actively motile.

The author of the present paper describes further experiments which, on the whole, confirm those previously carried out by Wenyon and O'Connor. He claims, however, that the eosin test for viability is not reliable and that in certain observations he has shown that cysts having an affinity for eosin, and others possessing no such affinity, have failed to initiate cultures when inoculated into suitable media. He has shown, however, by inoculation of faeces of flies previously fed on cyst-containing material into culture media, that the cysts passed by the flies are actually alive. Such viable cysts may be passed by flies at any time between 1 minute and 24 hours after feeding. By feeding flies on medicinal charcoal or carmine it has been shown that these substances are still being passed by the flies many days later, so that there is a possibility that protozoal cysts, if ingested in sufficient numbers, and provided they remain viable in the intestine, may be deposited by the flies on food after periods much longer than 24 hours.

[Whether the author's statement regarding the eosin is correct or not, the conclusions drawn regarding the carriage of intestinal protozoa by flies are the same as those previously made by other observers. It must, however, be impossible to state that every cyst inoculated into a culture tube has shown an affinity for eosin, while it is a common experience that presumably viable cysts may fail to give rise to cultures in suitable media.] *C. M. Wenyon.*

BREA (Mario M.), NIÑO (Flavio L.) & TAIANA (Jorge A.). Amibíasis hepatopulmonar. [**Amoebic Abscess of Lung and Liver.**]—*Bol. Inst. Clín. Quirúrg.* Buenos Aires. 1943. Feb. Vol. 19. No. 154. pp. 107–114. With 9 figs. English summary.

The patient was a man, 28 years of age, who seven years previously had had an attack of diarrhoea, probably dysenteric, and had suffered

with similar symptoms at intervals since then. During the seven months before he came under the author's care he suffered from pain in the right flank and hypochondrium and in the last two months in the right side of the chest also. He had a leucocytosis of 14,600 per cmm.; sputum blood-tinged and chocolate-coloured. Amoebae were not seen in it then, but they were later. X-rays showed a raising of the right side of the diaphragm, signs of abscess in the liver and a shadow in the right lung. Pus drawn from the lung contained *E. histolytica*. Injection of lipiodol proved the lung lesion to be continuous with that of the liver.

The patient was given subcutaneously 0·06 gm. of emetine hydrochloride daily to a total of 0·5 gm., followed by yatren, 45 pills orally in seven days, and 40 drops of 1 per cent. adrenalin. The result was most gratifying. Fever, pain and haemoptysis disappeared in a few days; the expectoration diminished in quantity from 300 cc. daily to 20 cc. in 20 days, the general condition and appetite improved and the patient put on weight. He left hospital 25 days afer his admission. By this time blood examination revealed red corpuscles 4,400,000, haemoglobin 84 per cent., white cells 8,900 per cmm., 77 per cent. polymorphonuclears. A month after he left hospital the cou se of emetine injections was repeated, and further observation and X-ray examination showed complete restoration to health.

H. Harold Scott.

MEDICAL RESEARCH COUNCIL. *Monthly Bull. Emergency Public Health Lab. Service.* 1943. May. Vol. 2. pp. 44–46. (*Not for sale.*)—**Giardia Lamblia Infection in Young Children.** [Summary appears also in *Bulletin of Hygiene.*]

An examination of young children in residential nurseries in Northamptonshire has shown that Giardia infection is widespread. Of 41 examined during epidemics of gastroenteritis 24, or 58·5 per cent., were infected, while of 118 healthy children only 36, or 30·5 per cent., were infected. Of 27 children suffering from diarrhoea 21, or 78 per cent., harboured the flagellate; of 130 who had normal stools 30 per cent. were infected. Other protozoa were also encountered. Thus in a series of 159 there were 60 cases of *Giardia intestinalis* infection, 10 cases of *Chilomastix mesnili* infection, 6 cases with *Entamoeba coli* and 3 cases with *Iodamoeba bütschlii*. It is noted that though *Giardia intestinalis* is the commonest intestinal protozoon found, the observations throw little light on the problem of the rôle of this flagellate in causing gastroenteritis, since an organism whose natural habitat is the upper part of the small intestine might be expected to appear in large numbers in the stools during attacks of diarrhoea. It is suggested that useful information might be obtained by studying the effect of mepacrine, which generally eradicates the infection in a few days. As a guide to dosage, that recommended by the League of Nations Commission as suitable for malaria is given, *viz.*:—

Age up to 5 years, 0·1 gm. daily.
Age 5–12 years, 0·2 gm. daily.
Age 12 years and over, 0·3 gm. daily.

The proviso is made that infants of 1 year and under are not treated.

C. M. Wenyon.

ROSSIER (P. H.) & DRESSLER (M.). Zur Frage der Lambliasis. [**On Lamblia Infections.**]—*Schweiz. Med. Woch.* 1943. Feb. 13. Vol. 73. No. 7. pp. 209–221. With 4 figs. [Numerous refs.]

This paper is a lengthy review of the literature on human lamblia infections, together with a description of 20 cases in adults which came under the authors' notice. The numerous symptoms, local and constitutional, which various authors have attributed to this infection are enumerated without any attempt being made at critical analysis. It is assumed that an hepatic syndrome exists, which is due to the invasion of the biliary passages by the flagellate [though, in fact, all reliable evidence indicates that such invasion rarely, if ever, occurs]. It is noted that the new remedies—atebrin, quinacrin, acranil—will easily eradicate the infection, thus affording opportunity of separating symptoms due to the flagellate from those due to other causes. The authors maintain that lamblia infections even when symptomless should be treated, as at any time acute symptoms may supervene. The paper, though a long one, gives no new information. *C. M. Wenyon.*

KUČERA (Kamil) & JIROVEC (Otto). Zur Kenntnis der menschlichen Darmparasiten in Mähren. [**Human Intestinal Protozoa in the Mähren District.**]—*Arch. f. Hyg. u. Bakt.* 1942. Vol. 128. No. 3. pp. 123–130. [Numerous refs.]

During the three years 1939–1941, the authors examined 623 patients in the Bat'a Hospital in Zlín in the Mähren District of Czechoslovakia for intestinal parasites. The examinations were carried out by examining wet and stained films of fresh and concentrated material and by culture methods. For protozoa 440 were examined and the following results in percentages were obtained:—*Entamoeba histolytica* 1·5, small races of *E. histolytica* (*E. hartmanni*) 1·5, *E. coli* 16·8, *Iodamoeba bütschlii* 1·5, *Endolimax nana* 5·2, *Dientamoeba fragilis* 0, *Trichomonas intestinalis* 0·2, *Chilomastix mesnili* 0·2, *Giardia intestinalis* 1·1, *Blastocystis hominis* 3·4. Parasitic worms were looked for in 623 patients, with the result that *Taenia solium* was discovered in 0·48 per cent., *T. saginata* in 3·8, *Dipylidium caninum* once, *Ascaris lumbricoides* in 4 per cent., *Enterobius vermicularis* in 4·5, *Trichuris trichiura* in 8·8 per cent. Mixed infections were commonly encountered. *C. M. Wenyon.*

LEPROSY.

AUSTIN (C. J.). **Central Leper Hospital, Makogai (Annual Report for 1941).**—*Fiji, Legislative Council. Council Paper No. 15.* 1942. pp. 8–10.

In 1941 the admissions numbered 59, 35 of which were neural and 24 lepromatous cases. The discharges numbered 47 and the deaths 34. Of 19 fairly advanced lepromatous cases 13 were in Indians, among whom earlier detection is required if good results are to be obtained; improved training of medical practitioners, regular examinations of school-children and all contacts of known cases, and the follow up of

discharged patients should greatly improve the position. In both types of leprosy a considerable majority of patients are in stage 2, and well over 50 per cent. are in an infective condition. This institution takes in cases from the Cook, Gilbert and other islands, and it is noteworthy that by far the highest percentage of arrested cases were among the Cook Islanders ; this is ascribed to the large proportion of very early cases sent by a Cook Island doctor who had been trained at the Makogai Leper Hospital. Among a total of 702 cases 111 (15·8 per cent.) were classed as " arrested " after being clinically and bacteriologically negative for two years, 47 were discharged during the year and 45 more are waiting examination by a medical board. Moreover, 154 (53·1 per cent.) of 290 " Lepromatous-2 " cases showed improvement during the year against 70·8 per cent. of 113 " Neural-1 " and 77·3 per cent. of " Neural-2." Of the 39 deaths 24 were due to leprosy (including sepsis and gangrene from trophic sores) and five were from pulmonary tuberculosis. Intramuscular injections of iodized chaulmoogra oil and intradermal injections of ethyl esters remain the routine treatment. Altogether, good progress is being made at Makogai under its experienced medical superintendent. *L. Rogers.*

DHARMENDRA & MUKHERJI (N.). **Seasonal Variations in the Activity of Lesions of Neuro-Macular Cases of Leprosy.**—*Leprosy in India.* 1943. Jan. Vol. 15. No. 1. pp. 7–14.

This paper records the results of an inquiry into the seasonal variations in the activity of neuro-muscular leprosy lesions, on the lines of that of LOWE and CHATTERJI in 1939 [this *Bulletin,* 1939, Vol. 36, p. 1015], which it confirms. The tuberculoid type was selected, in which alone such variations had been found in the earlier inquiry, and included 80 cases with recent exacerbations and 21 with the recent onset of thick red lesions. Only a few could be followed up for over a year. It was found that exacerbation of the lesions occurred in 65 per cent. of the cases during the four hot dry months of February to May and only 35 per cent. in the remaining eight months of the year ; the increased activity lasted for about six months. In the 24 bacteriologically positive cases the bacilli were found during the hot months, mostly in April and May. During the phase of activity the lepromin test showed strong reactions. Of 37 cases which remained under observation for from one to three years, in seven the increased activity was again observed in the second or third year, but it was less marked than in the first year.

In discussing the causation of the seasonal exacerbations the authors point out that observations in other countries showed exacerbations in the spring and autumn in Russia and in the colder months of December and January in Nigeria, so climatic conditions do not explain the phenomena. Nor are they related to increased consumption of colocasia, as has been suggested, for more is consumed in Eastern Bengal with little leprosy and less in Western Bengal with high leprosy incidence. The causation of these seasonal variations is thus not clear. *L. Rogers.*

LEPROSY IN INDIA. 1943. Jan. Vol. 15. No. 1. pp. 3–6. [16 refs.]—**Colocasia and Leprosy.**

" *Conclusions.*—Several years ago one worker suggested that in Africa the eating of colocasia (taro) might precipitate the appearance

of leprous lesions in a person with a latent leprous infection and might aggravate such lesions if already present. This effect was attributed to certain substances present in taro. Seasonal variations in the consumption of taro were considered to be related to seasonal variations in the manifestations of leprosy which were observed.

"The evidence produced in support of the theory was very slight and no further facts in corroboration have been produced by the original workers or by any other worker.

"The suspected substances are, it is believed, removed by the prolonged boiling usually given. Moreover seasonal variations in leprosy occur in several parts of the world independent of the consumption of colocasia.

"The general opinion of experienced workers is that the theory has no sound foundation and that the consumption of colocasia as such plays no part in the causation or aggravation of leprosy.

"While colocasia is a starchy root which is not of outstanding nutritive value it may form a useful supplementary article of diet. There is no valid reason why its production and consumption should not be encouraged in order to increase food supply in times and areas of food shortage."

HAYTHORNTHWAITE (H. M.). **Lactoflavine for Bullae, and Closed Plaster for Trophic Ulcers.**—*Leprosy in India.* 1943. Jan. Vol. 15. No. 1. pp. 20–22. With 2 figs.

This note deals with two points of practical importance in the treatment of leprosy. Crops of bullae leading to the formation of painful ulcers may cause much distress. In view of lactoflavine having been recommended in the treatment of pemphigus the author has used it in 24 cases of bulla formation with success in every case. Injections of 2 cc. lactoflavine (B.D.H.) four or five times in the course of a year were effective in keeping five long-standing cases free from these lesions; three others cleared up after one to three injections. The condition is not associated with other signs of vitamin B_2 deficiency.

His other point is that, in the absence of hospital accommodation, great relief was afforded, in cases of perforating ulcers of the foot without bone disease, by a light plaster support. *L. Rogers.*

HELMINTHIASIS.

ELLIOTT (W. G. M.). **Phenothiazine Treatment of Multiple Intestinal Helminthic Infestations.**—*Jl. Roy. Army Med. Corps.* 1943. Mar. Vol. 80. No. 3. pp. 156–159.

The author, whose earlier successful treatment of 18 cases of dracontiasis in West African troops by injections of an emulsion of phenothiazine have been reported [this *Bulletin*, 1942, Vol. 39, p. 778] has now treated 26 cases of infestation with various helminths in West African troops with phenothiazine given by the mouth. None of the patients showed any clinical evidence of toxic effects (*i.e.* no headache, vomiting, nausea, diarrhoea, jaundice or abdominal discomfort), but the author does not say whether he made any examinations of the blood or not. Many of his patients suffered from vitamin deficiencies,

especially lack of vitamin B_2, and many had yaws, chronic malaria, filariasis, dracontiasis or schistosomiasis. On admission they were given a semi-solid diet and the fluid intake was discouraged; each day 2 ounces of glucose, 2 ounces of Bemax, and a teaspoonful of Marmite were given. The first evening half an ounce of sodium sulphate was given, and this was repeated next morning. The first stool was sent to the laboratory and 4 gm. of phenothiazine were given morning and evening for two days. On the third morning 8 gm. were given. Four hours after this last dose the patients resumed a full diet. If three consecutive stools were free from parasites after this treatment, the patients were discharged and asked to report for a check up a month later. If further treatment is necessary, the author recommends that no more phenothiazine should be given for three weeks (apparently he means for three weeks after the first treatment). If toxic signs develop the drug should be stopped. Infants and children should be observed for a week after treatment.

Elliott concludes that this treatment eliminates *Trichuris trichiura* and *Strongyloides stercoralis* and has "undoubted value" for the treatment of *Ancylostoma duodenale* [contr. MANSON-BAHR, this *Bulletin*, 1942, Vol. 39, p. 6, who found that it had no effect on this species] and of *Taenia saginata*; it has little action on *Chilomastix mesnili*.

[The results of recent trials conducted by the Agricultural Research Council, shortly to be published, indicate that, when graded doses of 5–50 gm. of phenothiazine were given to a large number of sheep, only the higher doses (40–50 gm.) decreased the numbers of *Strongyloides papillosus* and *Trichuris*. Statistical analysis of the results suggested that the tapeworm *Moniezia*, and probably the nematode *Nematodirus* also, were more numerous among lambs heavily dosed with phenothiazine. Possibly the removal of other competing species by the phenothiazine helped the survival of these two species and possibly lower doses (20–30 gm.) helped the survival of *Trichuris* and *Strongyloides papillosus*. KAUZAL (*Jl. Counc. of Sci. and Ind. Res.*, 1941, Vol. 14, p. 218) found that a dose of 0·6 gm. per kilo. live weight had no effect on *Strongyloides papillosus* of lambs 4–5 months old and none on its egg-production. Much more evidence, derived from the treatment of a sufficiently large number of patients, followed by careful checking of the results by approved helminthological methods, is required to establish the effect of phenothiazine on the nematodes of man. For the risks associated with the administration of phenothiazine to man and animals, see this *Bulletin*, 1942, Vol. 39, pp. 861–862.]

G. Lapage.

KOPPISCH (Enrique). **Manson's Schistosomiasis.**—*Jl. Amer. Med. Assoc.* 1943. Mar. 20. Vol. 121. No. 12. pp. 936–942. With 6 figs. [25 refs.]

No planorbid snail in North America has yet been proved capable of acting as the intermediate host of Schistosoma [*cf.* BLUM and LILGA this *Bulletin*, 1943, Vol. 40, p. 552], but there is no certainty that none exists until an exhaustive survey of N. American snails has been made.

The geographical distribution and life history of *Schistosoma mansoni* and the prevention of the disease are briefly discussed. Most of the paper is devoted to the pathology and clinical manifestations. Controversial points, such as the route taken by the metacercariae from the

skin to the lungs, the means by which the eggs get into the tissues from the blood vessels in which they are laid and how they reach the lumen of the intestine and the various organs of the body, are discussed.

Clinically the disease is divided into three stages. In the early stage, when the metacercariae migrate to and mature in the branches of the portal vein in the liver, there are usually no symptoms, except itching a few hours after exposure to infested water. The intermediate stage begins when the worms begin to lay eggs, about 40 days after exposure to infestation. During this stage eggs are accumulating in the liver and other organs. In the liver they will eventually cause irreversible cirrhosis, with the formation of pseudo-tubercles round the eggs; chronic colitis, with or without ulceration and fistulae, is being established; splenomegaly with diffuse fibrosis of the pulp of the spleen and changes in other organs due to the presence of the eggs are also in progress. Diagnosis and treatment are important during this stage, before an irreversible hepatic cirrhosis is established. In the late stage the average patient shows hepatic cirrhosis and the condition of the liver decides the prognosis, rather than the colitis or the complications (salpingitis, oophoritis, myelitis, pulmonary arteritis). Splenomegaly, ascites, anaemia, cachexia, are established, abdominal discomfort and eosinophilia may persist, fever may reappear for a few days or weeks, but diarrhoea may be absent for long periods. Ova may be absent from the stools. Complement fixation, precipitin and cutaneous tests may help diagnosis.

Referring to differences between the disease in Porto Rico and in Egypt, the author says that there is, in Egypt, a relative predominance of papillomatous formations, especially in the lower rectum, and of colitis without cirrhosis. In Porto Rico the infestation is milder, probably because Porto Rico people encounter less chances of heavy infestations. In Egypt more people probably go untreated or are insufficiently treated, because vastly larger numbers are infested, so that the detection of cases and their examination after treatment are more difficult. *G. Lapage.*

YARWOOD (G. R.) & ELMES (B. G. T.). *Paragonimus* **Cyst in a West African Native.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1943. May. Vol. 36. No. 6. pp. 347–351. With 3 figs. on 2 plates.

The authors think that the occurrence of paragonimiasis in Africa has not received general recognition; they here record a Nigerian case.

The patient was a male aged 23, born in Okarki, S. Nigeria, where he had lived all his life until 18 months before the authors saw him. He was accustomed to eat fish, shrimps, snails, crabs and crayfish from the creeks and rivers near his home; these were roasted, but in Nigeria this means that they may be almost raw. In 1931 he had a "fit" for about two minutes, but retained consciousness while it lasted. In May 1940 a small swelling appeared over the temporal bone above the left ear, and in July 1941 another on the left side of the neck. Early in 1942 the swelling gradually increased without earache, until, in June 1942, he had jabbing pain in the left ear with high-pitched tinnitus and impaired hearing. During the six months before September 1942, when the authors saw him, he had had frequent attacks of misty vision lasting one or two minutes, usually early in the morning.

When he was seen the patient had a painless fluctuant swelling measuring 5 by 3 cm. in the upper third of the left sterno-mastoid; there was no enlargement of the glands, no otitis externa, the ear drum was normal and there was no oral trouble. Operation revealed a thin-walled cyst deep in the muscle of the levator scapulae which extended back to the base of the skull. The pus from the cyst contained numerous eggs "indistinguishable from those of Paragonimus"; they were broadly oval, pale yellowish-brown, without segmentation of the contents and without any noticeable thickening of the shell at the pole opposite to the operculum, such as is usually described in the eggs of *P. westermanii*. They measured, after fixation in 10 per cent. formol saline, 62 by 40 microns. The authors think that, even when allowance is made for shrinkage, this size is smaller than that given for the eggs of "Paragonimus species," *i.e.* 70–90 by 45–55 microns, and they think they may possibly have observed a new species or variety occurring in West Africa. [BELDING, 1942, Text-book of Clinical Parasitology, gives 73–118 by 46–67 microns as the size of the eggs of *P. westermanii*.] No adult trematodes were found in the cyst, but this was ruptured during the operation and was not removed complete. The incomplete cyst measured 5 by 4 cm. and had a wall 1 or 2 mm. thick. The cyst consisted of an outer zone of collagen fibres with occasional bundles of striped muscle, plenty of small blood vessels, scanty inflammatory cells, an occasional foreign body giant cell and few eggs; and an inner zone of vascular granulation tissue mixed with collagen fibres richly infiltrated with eggs and inflammatory cells; eosinophils were scanty in this and also in the pus. In the blood there were 8 per cent. of eosinophils, 61 per cent. of lymphocytes and 29 per cent. of polymorphonuclears; but high lymphocyte counts are common in Nigeria. The sputum, taken after enforced coughing, was normal. The chest and alimentary canal were normal. The left ear drum was normal, but the hearing was considerably impaired, bone conduction being greater than air conduction. There was right homonymous hemianopia and impaired vision of the whole right eye. Pupil reflexes, fundi and cranial nerves were normal. There was no nystagmus, ataxia or dysdiadochokinesis, but slight Rombergism to the right side. The arms and legs of the right side showed diminished muscular power and there was hypotonia of the left side. All the deep reflexes of the left arm were diminished and the left knee jerk was only elicited after reinforcement. Ankle jerks, plantar reflexes and radiology of the cranium were normal.

The authors suggest that the flukes caused multiple lesions of the central nervous system and also migrated into the region of the left ear.

G. Lapage.

CHANDLER (Asa C.). **Studies on the Nutrition of Tapeworms.**—*Amer. Jl. Hyg.* 1943. Mar. Vol. 37. No. 2. pp. 121–130. [16 refs.]

After remarking that there is no experimental verification of the common view that tapeworms depend for their food on digested or semi-digested substances in the intestines of their hosts, the author reviews the experimental work that has been done on the nutrition of tapeworms. This indicates that starvation of the host, and especially removal of carbohydrates from its food, reduces the egg production and glycogen content of tapeworms in it. HAGER [*Iowa State College Journal of Science*, 1941, Vol. 15, pp. 127–153] found that elimination

of the vitamin B complex from the diet of rats infested with *Hymenolepis diminuta* caused practically complete inhibition of the egg output; elimination of vitamin G only has the same effect; but elimination of vitamin B_1 only caused no significant decrease of egg production. WARDLE [*Physiol. Zool.*, 1934, Vol. 7, p. 36], GREEN and WARDLE [*Canadian Jl. Res., D.*, 1941, Vol. 19, p. 240] and MARKOV [*C. Rend. Acad. Sci. U.R.S.S., Dok.*, 1939, Vol. 25, p. 93] all kept tapeworms in artificial media. WARDLE thinks that glucose is the only carbohydrate needed by tapeworms, and that they synthesize it into glycogen and store it in the cells of the parenchyma, that they cannot synthesize glycogen from amino-acids because their respiration is not aerobic and that they may need only simple amino-acids and no fats. Chandler suspected that tapeworms get part of their food from the mucosae of their hosts, because immature tapeworms, even those, which, like *Cysticercus fasciolaris*, develop some of the strobila in the bladderworm stage, always take food from the host's tissues and are usually not bathed in blood or body cavity fluids, but are in the liver, muscle, brain, under serous membranes or even in a thick connective tissue capsule (hydatids). Also adult tapeworms are not always confined to the lumen of the intestine. Various species are mentioned which may be found in the bile ducts or body cavity. Further, host specificity is rather marked among tapeworms, which one would not expect if they did not depend partly on the host's tissues for food.

Working with *Hymenolepis diminuta* in albino rats, Chandler tried the effects of elimination of proteins and vitamins from the diets of the hosts. Details of all the diets are given.

The first experiment indicated that elimination of protein from the host's diet had no evident effect on the growth or reproductive capacity of the tapeworms. Elimination of all vitamins had no effect on the growth or establishment of the tapeworms in the male rats, although there was some reduction of their reproductive capacity. But there was a striking failure of the tapeworms to establish themselves in the female rats deprived of all vitamins whether or not these were given protein as well. Of the few that did establish themselves, those in the rats deprived of vitamins but given protein were markedly smaller (only 50 mm. long) than those in rats deprived of both protein and vitamins (745 and 762 mm. long). On the other hand, tapeworms in rats given vitamins but no protein were larger than those in the controls, and in one female of this group tapeworms bigger than any the author had seen were found. They were also bigger in males deprived of both protein and vitamins than in the controls. Experiment 2 confirmed the facts that lack of vitamins in the host diet has a marked effect on the establishment and growth of tapeworms in female, but not in male rats, and that most of those that did establish themselves in female rats were small.

Experiment 3 indicated that complete lack of carbohydrate from the host's diet caused marked reduction of the establishment of the tapeworms and very severe stunting of their growth, the total average length of worms per rat being reduced to one-tenth of that of worms in rats on a normal diet. Reduction of carbohydrate to 5 gm. a day produced a slight but significant decrease in length and width of the tapeworms. Lack of the fat soluble vitamins A, D and E had no effect whatever on the establishment of the tapeworms in the host or on their growth, nor had lack of vitamin B_1. Lack of the vitamin G complex did not affect the establishment of the tapeworms, but it

caused a marked stunting of their size, nearly equivalent to that caused by lack of carbohydrate. This confirms HAGER's results.

The tapeworms were thus totally independent of protein in the host's diet; some of them found in rats deprived of protein were actually larger than any that the author had previously seen. It is evident that they absorbed protein directly from the intestinal mucosa of the host; this may explain the stunting effect of overcrowding which has often been reported, because this would interfere with surface contact of the tapeworms with the mucosa.

The increase in size of tapeworms in rats deprived of protein only was not expected. This, and also the better growth of the tapeworms in rats deprived of protein but given vitamins than in rats deprived of vitamins only may be due to failure of these rats to use some part of the vitamin G complex, so that more is available for the worms. Like REID [*Supp. to Jl. Parasitology*, 1940, Vol. 26, p. 16] Chandler thus found that *H. diminuta* cannot get enough carbohydrate from the mucosa and is very sensitive even to partial restriction of it in the diet. Reid is probably right in assuming that the effect on the tapeworms of starvation of the host is due to deprivation of carbohydrate. *H. diminuta* is independent of fat-soluble vitamins A, D and E and of B_1, but in female rats it is affected by lack of some part of the vitamin G complex. It may be able to get enough of the vitamin B complex from the host's mucosa, because single worms in hosts deprived of protein grew to normal size.

The conclusion is thus warranted that tapeworms get the bulk of their carbohydrate from their host's intestinal contents, but can absorb nitrogenous substances and probably B vitamins to a limited extent direct from the host's intestinal mucosa. If this is so, the common idea that tapeworms produce their effects by robbing the host of its food and excreting toxins should be replaced by the view that the nervous symptoms, gastro-intestinal troubles, loss of weight and general weakness may be due, not to the absorption of toxins, but to absorption of vitamins, protein and possibly hormones and other substances from the host's intestinal mucosa. Tapeworms often produce no symptoms in well-nourished individuals and their effects vary in different individuals. Possibly Diphyllobothrium absorbs the intrinsic factor which converts the extrinsic factor contained in meat and yeast (which is possibly part of the vitamin G complex) into an anti-pernicious-anaemia factor, so that pernicious anaemia results in individuals who have not enough of either the extrinsic or intrinsic factors. *G. Lapage.*

MUKERJI (A. K.) & MAPLESTONE (P. A.). **Preservation of Hookworm Ova in Faeces.**—*Indian Med. Gaz.* 1943. Mar. Vol. 78. No. 3. pp. 136–141.

The authors wished to find a preservative which would keep hookworm eggs long enough for them to be sent from distant places to a laboratory; they decided that preservation for 3 weeks would be sufficient for this purpose. Egg counts were done on faeces 3 to 4 hours after they had been passed: 4 cc. samples, in paper containers, were then dropped into phials containing 20 cc. of the preservative being tested; the phials were shaken to free the faeces from the paper containers and they were left for 3 weeks. Final counts were then made.

The following preservatives all proved to be unsatisfactory: antiformin made with the proprietary chlorine preparations called Chlorion and Perchloron, Scott's antiformin, paranitrophenol, acriflavine, methylene blue, brilliant green, gentian violet, mercurochrome, cyllin, Dettol, thymol, formalin, formalin-saline. While trying formalin-saline it was noticed that the eggs kept well in a 1 per cent. NaCl. control solution. This was therefore tested, but it was found that the *p*H fell during the 3 weeks and that, if it fell more than 0·3, loss of eggs began; the less the fall of *p*H, the less the loss of eggs. Reduction of *p*H was due to fatty acids resulting from imperfect carbohydrate digestion due to hookworm disease and to excess of fats in the diet. Buffered NaCl solutions did not maintain the *p*H and no better results were obtained by the use of sodium bicarbonate.

Finally it was found that dilution of the stool with the salt solution to 1 in 30 solved the difficulty. When this dilution was adopted, instead of the 1 in 6 dilution used for the earlier trials, eggs were not lost and sometimes the final counts were higher than the initial ones. Longer trials showed that the eggs begin to degenerate after about 28 days in 1 per cent. NaCl solution. In the field stools can be collected in 3 cc. paper containers, which are dropped into sample bottles containing 87 cc. of 1 per cent. salt solution, or the same amount of stools can be measured into the bottles by displacement. The bottles are well corked, the corks are tied to the necks of the bottles and these are sent to the laboratory for counting. After 3 weeks in this solution eggs look quite fresh, only occasional degenerate ones being seen (only 34 out of 2,820 eggs counted in 23 experiments were degenerate).

G. Lapage.

BECMEUR (A.). Deux ans de lutte contre l'ankylostomiase dans les mines de l'Office Chérifien des phosphates. [**Two Years of Measures against Ankylostomiasis in the Mines of the Sherifian Phosphate Service.**]—*Bull. Inst. Hyg. Maroc.* 1941. N.S. Vol. 1. pp. 45–53.

Ankylostomiasis was first found in the phosphate mines at Khouribga in two European workers in 1937. The author gives figures of examinations of the workers in these mines carried out in 1938, 1940 and 1941, and concludes that ankylostomiasis had at the end of 1941 disappeared as a result of sanitary measures and treatment of infested persons. At the end of 1941 only 109 lightly infested healthy carriers were found with less than 10 eggs per cc. of the faeces; these would be no danger to the staff of the mines and would be spontaneously cured in two or three years, which is the normal life of ankylostomes. Examination of the miners, sanitary measures and treatment of infestations likely to menace health will, however, continue. *G. Lapage.*

PASTERNACK (Joseph G.). **Filarial Epididymofuniculitis.**—*Arch. Pathology.* 1943. Mar. Vol. 35. No. 3. pp. 414–419. With 2 figs.

The author calls particular attention to genital complications or sequelae of filarial infection because returning American troops "will have diseases unfamiliar to American physicians," and he warns the latter so that they may be on the look-out for these filarial conditions, using the same words as Sir Philip Manson-Bahr does in Manson's Tropical Diseases, that "patients with chronic swellings about the

spermatic cord, testis, scrotum and groin who have been in the tropics should always be regarded as possibly filarial." [The quotation is not acknowledged by the author either by reference or even by the use of inverted commas.] Readers with wide tropical experience will not entirely endorse the statement that filariasis, due to *W. bancrofti* is second only to malaria in prevalence.

The author details two cases, one in a native aged 37, from the Cape Verde Islands, the other in a white seaman from Martinique, with nodular lesions of the epididymis, a thickened beady spermatic cord and nodules of the testis. Histologically, there was much fibrosis, thickened capillaries, lymphangiectasis and some granulomatous tissue—in brief, an "obliterative granulomatous endolymphangitis." In the sections remains may be seen of dead filariae, partly calcified. Clinically, symptoms may be few—fever, pain and chills in the earlier stages, later swelling and hardness of the spermatic cord and swollen, tender epididymis—all these in the acute or subacute stages; in the chronic stage, merely a dull aching pain and swelling of the scrotum.

H. Harold Scott.

SUMMERS (William A.). **Experimental Studies on the Larval Development of *Dirofilaria immitis* in certain Insects.**—*Amer. Jl. Hyg.* 1943. Mar. Vol. 37. No. 2. pp. 173–178.

TORRES ESTRADA (Antonio). **Ophthalmoscopic Observation on Microfilarias in the Vitreous of Patients Infected with Onchocerciasis.**—*Amer. Jl. Ophthalm.* 1942. Dec. Vol. 25. No. 12. pp. 1445–1448.

Patients with onchocerciasis often report that they see tiny worm-like bodies in their eyes. SILVA, in 1925, merely by illuminating the fundus with a flat mirror, saw microfilariae as very mobile, very refringent bodies with golden reflections; with the Gullstrand ophthalmoscope he saw the shadows of the microfilariae on the retinal surface. OCHOTERENA [this *Bulletin*, 1930, Vol. 27, p. 992] and STRONG [*ibid.*, 1932, Vol. 29, p. 82] found microfilariae in sections of the conjunctiva, cornea, choroid and retina [*cf.* also SEMADINI, this *Bulletin*, 1943, Vol. 40, p. 616]. TORROELLA first used the slit-lamp microscope [*cf.* also SEMADINI, above] for the detection of microfilariae and observed them in the anterior chamber. But the corneal microscope can be used only in well-equipped laboratories; in order to see the posterior portion of the vitreous a Koeppe microscope and a special contact glass must be used. The examination fatigues the patient and the microfilariae are difficult to see, because they are very thin and refringent, very mobile and are scarce in the anterior chamber. They are best seen with low magnifications and can be seen with a hand lens.

The author found that microfilariae in the vitreous are most easily seen with the electric direct-image ophthalmoscope using a +20 to +40 diopter lens; the refraction of this, combined with that of the refraction system of the eye, makes possible observation of the microfilariae in fine detail. The punctate keratitis which is often present does not interfere, because it appears late in the disease and begins at the periphery of the cornea; nor do exudates in the pupil due to iritis.

Microfilariae seen in the anterior chamber with the corneal microscope, *i.e.* by direct light, look like white, very fine, active filaments with golden reflections. Microfilariae seen with the ophthalmoscope,

i.e. by transmitted light, look like very fine black filaments on a reddish background ; they reminded the author of the appearance of mosquito larvae in water and patients also use this simile ; they only look refringent, with golden reflections (*i.e.* as they appear by the slit-lamp microscope) when they come very close to the posterior part of the lens. The observation is best made with the pupil dilated.

The electric ophthalmoscope is simple ; examinations with it can be done anywhere ; the general practitioner and visiting nurses can detect microfilariae with it. Microfilariae seem to be more abundant in the vitreous than in the anterior chamber and may be seen in the vitreous early in the disease. They may be found there in patients in whom none is found in the anterior chamber and in whom biopsy of the skin has been negative. The author examined 11 cases of onchocerciasis and found microfilariae in all of them by opthalmoscopy of the vitreous ; microscopy of the anterior chamber revealed them in four of these cases only ; six of them had keratitis. In other words, vitreous ophthalmoscopy is better than corneal microscopy.

The microfilariae are negatively phototactic, being more apparent in the anterior chamber by night than by day and more numerous at the periphery of the pupillary field during examination than within it ; at the beginning of the examination, especially if the patient has stayed in a dark room, some are often seen in the centre of the field, but a few minutes later they have fled to its periphery. [Nematode larvae usually behave thus on a slide under the microscope. They prefer diffuse light, those living on pastures being most active at dawn and dusk, so that infestation of farm animals is more likely at these times.]

G. Lapage.

KUITUNEN-EKBAUM (E.). **The Incidence of Enterobiasis in Toronto.**—*Canadian Med. Assoc. Jl.* 1943. Mar. Vol. 48. No. 3. pp. 229–231.

" A survey of enterobiasis in Toronto showed the incidence of 60% in 300 children and 52% in 56 adults examined.

" In 29 of the 34 families examined either all members of the family or the majority of them were infected with pinworms. Five families examined were free of infection.

" The NIH swab was used with an average of 6 swabs per person."

HEADLEE (William Hugh). **Pinworm Infections among Patients of an Indiana Hospital for Children.**—*Amer. Jl. Trop. Med.* 1943. Mar. Vol. 23. No. 2. pp. 281–284. [10 refs.]

" Perianal scrapings, collected by means of the N.I.H. cellophane-tipped swab, were examined from 240 patients of the James Whitcomb Riley Hospital for Children. These included 128 males and 112 females, with ages from 21 months to 18 years. They were residents of both urban and rural areas throughout the state and came from 71 of the 92 counties. Only one perianal scrapings preparation was examined from each patient. A total of 39 individuals (20 males and 19 females), or 16·3 per cent., were found to be infected with the pinworm, *Enterobius vermicularis*. The corrected incidence, on the basis of the examination of seven swabs, was 24·7 per cent. Eosinophil counts from both positive and negative individuals were analyzed. There seemed to be no correlation between the eosinophil count and the presence or absence of an infection with *Enterobius vermicularis*."

PERRIN (Tomás G.). Algunos estudios sobre triquinosis ignoradas. [**Studies on Undiagnosed Trichiniasis.**]—*Rev. Med. Trop. y Parasit.* Habana. 1942. Sept.–Oct. Vol. 8. No. 5. pp. 59–64. With 5 figs. [28 refs.]

In the diaphragms of 25 of 200 cadavers (12·5 per cent.) of persons without a clinical history of trichiniasis the larvae of *Trichinella spiralis* were found by direct microscopical examination. The number of larvae per gm. of muscle varied between 0·5 and 27. The proportion of 0·01 larva per gm. is regarded as simple "zoological trichiniasis" and values higher than this suggest clinical trichiniasis. Of the 25 positives 15 were men and 10 women, the ages varying from 19 to 87, although most of them were over 30.

Working with the Bachman-Bozicevich antigen (prepared without phenol and diluted 1 in 10,000) supplied by the American National Institute of Health, the author obtained positive skin reactions in 18 out of 125 persons who had not shown previous signs of trichiniasis, so that 14·4 per cent. were probably infested. Of 14 of these 18 positives, 10 had an eosinophilia of 5–8 per cent. When 8 medical men were skin-tested, 3 were found positive: one of them had suspected, a year and a half earlier, that he had trichiniasis. A year after receipt of the antigen, injection of 0·04 cc. (double the dose given in the earlier tests) gave positive results in 3 cases of trichiniasis, but negative ones in 4 cases of infestation with Trichocephalus, 2 with Ascaris, 2 with Enterobius and one with Ancylostoma. After 16 months in the refrigerator the antigen gave positive tests in 2 cases suspected of trichiniasis, with eosinophilia of 13 and 23 per cent. respectively. After 25 and 26 months in the refrigerator one patient with the clinical picture of trichiniasis and another suspected of the disease both gave negative skin tests. Probably it was then inactivated by age and cannot be kept longer than 18 months. The high percentage of cases now known in Mexico justifies measures for the control of pig breeding (prevention of the access of rats, the cooking of food given to pigs, etc.) and education of the people in the proper cooking of pig meat. *G. Lapage.*

DEFICIENCY DISEASES.

HEILIG (Robert). **Clinical Experiences on Vitamin Deficiencies in Mysore.**—*Indian Med. Gaz.* 1943. Mar. Vol. 78. No. 3. pp. 129–134. [53 refs.]

"In India," states the author, "at least outside the big cities and research centres, nutritional deficiencies are far too rarely recognized as such, and still more rarely is the deficient factor or group of factors properly determined." From investigations carried out in many parts of the country it may be justly concluded that vitamin A and B deficiency is common, that there is lack of animal protein, calcium and fat; vitamin C deficiency is noticeable in famine areas and vitamin D where the purdah system is in force. The author then proceeds to speak of various syndromes he has observed in Mysore, attributable, in part at least, to one or more of these deficiencies, backing his opinion by references to the literature, and he concludes that the people are

"living on the borderline of numerous deficiencies" and that any additional strain may precipitate symptoms. Ankylostomiasis is very rife and, if vitamin B is wanting, severe anaemia may appear. To increase natural resistance is not merely a question of additional income; intake of vitamin C (Jamshedpur is given as an example on the authority of K. MITRA [see *Bulletin of Hygiene*, 1940, Vol. 15, p. 619]) was found to be higher among the poorer classes than among the well-to-do. Hospital patients often refuse milk and milk products because, they believe, they "cause cold and swelling all over the body"; they prefer grossly overcooked vegetables. It will be necessary to educate the people in the right use of foodstuffs and the proper preparation of them—a laborious undertaking. *H. Harold Scott.*

COFIÑO UBICO (Ernesto) & ARGUEDAS KLÉE (Gustavo). Contribución al estudio de ciertos edemas de la infancia. (Sindroma debido a carencia alimenticia múltiple.) [**Study of certain Forms of Oedema in Children. Syndrome due to Diet Deficiency.**]—*Mem. d. V. Congr. Méd. Centroamericano, San Salvador, 5–12 Nov., 1938.* pp. 543–580. With 10 figs.

The authors have carried out a serious piece of work, investigating from the clinical and laboratory sides an important problem. They have observed many children between one and six years of age with digestive disorders, changes in the skin and hair and modification in the blood proteins. A similar condition has been described in San Salvador, Costa Rica, Mexico and Cuba. It is common among the poorer classes. It is due fundamentally to diet defects, notably in fats, proteid and vitamins, with excess of carbohydrates, and cannot be ascribed to any one deficiency in particular. Examination of the blood reveals more or less important diminution of total protein, loss of albumen and increase in globulin. The method of determination of blood protein is described in detail, using small quantities (1–2 cc.) of serum.

Treatment consists in blood transfusion and change to adequate diet. Transfusion should be started at the first sign of the oedema, for the more promptly it is used the more rapid and complete the cure; it benefits in cases apparently desperate and is to be repeated "as often as necessary to produce appreciable benefit." Improvement of the diet should start with increase of proteins of animal origin, then of rats. Care is needed because the alimentary tract is very easily upset and vitamins B and C are all-important. *H. Harold Scott.*

SPRUE.

INGELFINGER (Franz J.). **The Diagnosis of Sprue in Nontropical Areas.** —*New England Jl. of Med.* 1943. Feb. 11. Vol. 228. No. 6. pp. 180–184. With 2 figs. [28 refs.]

Sprue and sprue-like conditions are not rare in northern latitudes, but complicating features are often so prominent that the underlying disorder is not immediately recognized.

The outstanding feature is excess of output of faecal fat. The general opinion is that this is due to malabsorption of lipids, but it

is more likely that patients with this disease absorb all substances slowly, even water and gases, glucose and amino acids. The small intestine is long enough to compensate for delayed absorption rate of glucose and amino acids so that these substances do not appear in excess in the faeces. Fats are much more slowly absorbed and delayed lipid absorption causes fatty substances to be spilled over into the colon.

Patients who have suffered from extensive granulomatous disease of the small intestine, resections, or short circuit of the small intestine also have steatorrhoea, but in these cases curtailment of the absorbing surface is responsible.

Of the four patients forming material for this study two never passed typical greasy stools, though they were found to have steatorrhoea. Abdominal distension has usually been ascribed to intestinal fermentation, but a better explanation is provided in the marked loss of intestinal tone, which prevents proper propulsion, elimination and absorption of gases.

The anaemia of sprue may simulate that of pernicious anaemia or may be hypochromic and microcytic. Two of these patients had microcytic, and two macrocytic, anaemia. In sprue, liver extracts benefit the anaemia, especially if severe, but the amount necessary is two or three times as great as that needed in pernicious anaemia.

Each of the four patients had tetany. Formerly, hypocalcaemia was ascribed to formation of insoluble calcium soaps in the intestine. The *p*H of the small bowel, however, rarely rises above 7·5, and it is known that in a medium with a *p*H of less than 8, many soaps do not form; hence the suggestion that faulty calcium absorption is a secondary result of poor absorption of vitamin D offers a more reasonable explanation of hypocalcaemia. Thus massive vitamin D therapy will raise the serum-calcium level in patients with steatorrhoea. On the other hand, increasing the fat in the dietary is followed by an increased output of faecal calcium.

In spite of low serum calcium content, none of the patients showed definite osteoporosis of the long bones, and the serum phosphatase levels were normal.

One patient, who was admitted to hospital with haematuria, developed purpura with bleeding from the nose and mouth and formation of extensive purpuric areas over the body. The prothrombin time had dropped to 1 per cent. of normal. The cause of this deficiency is probably the same as that of hypocalcaemia and is due to failure to absorb vitamin K.

Patients with tropical sprue usually have striking evidence of deficiency of the vitamin B complex, especially of nicotinic acid and riboflavin. One patient exhibited cheilosis, angular stomatitis and glossitis; also prominent was the deep fiery red colour of the mucosa of the proximal and dorsal portions of an ileostomy which had been performed. Administration of thiamin hydrochloride (10 mgm. three times daily intramuscularly) aggravated the condition. Thereupon he was injected with a preparation of vitamin B complex (3 mgm. of thiamin, 10 mgm. nicotinic acid, 0·5 mgm. riboflavin, 0·45 mgm. pyridoxine and 1·68 mgm. pantothenic acid per cc.). 2·5 cc. of this preparation daily, together with 2·5 cc. of crude liver extract, resulted in the disappearance of these symptoms. These observations suggested that the patient was unable to absorb the vitamin B fractions when given by the mouth.

Symptoms of vitamin A deficiency were also present. Two patients complained of night-blindness. The fasting levels of vitamin A in the plasma were strikingly decreased in three patients. After a large dose (250,000 I.U.) of vitamin A by mouth little absorption occurred, as far as could be ascertained by the plasma levels. Low carotene values in the blood are significant in the diagnosis of steatorrhoea, but low vitamin A values are found in other disorders. *P. Manson-Bahr.*

HAEMATOLOGY.

MORAGUES (Vicente). Anemia semilunar o de celulas falciformes. [**Sickle Cell Anaemia.**]—*Rev. Med. Trop. y Parasit.* Habana. 1941. Sept.–Oct. Vol. 7. No. 5. pp. 90–95. With 7 figs. [35 refs.]

A good general account of this curious condition, illustrated by reports of two cases and of the post-mortem findings, but it adds little to the knowledge we have already. The author's investigations show him that sickle cells, without anaemia, are a family and hereditary characteristic of 7·5 per cent. of North American negroes, while sickle-cell anaemia occurs in only 0·2 per cent. The cases he describes in detail were in a boy of seven, who had been ill for five years, and in a woman of 28 years.

The following statements are based on reports in the literature and on the author's own study. The number of corpuscles ranges between one million and three million per cmm., some 90 per cent. being sickle-shaped; haemoglobin 40–50 per cent.; there is leucocytosis between 15,000 and 40,000. Normoblasts are many and reticulocytes much increased, platelets normal or slightly increased. Males are affected about twice as often as females; the average age of patients is 12 years. The blood plasma is yellowish; van den Bergh direct is negative in most, indirect positive in nearly all. Jaundice is present and, in many, urobilinuria. Patients are very susceptible to infection and death from intercurrent disease is common, so the pathological findings are often complicated by lesions set up by the secondary or terminal affection. The heart is usually hypertrophied, the liver enlarged and congested, the Kupffer cells phagocytize many of the sickle red cells. The spleen *in children is much enlarged in the early stages of the disease* [our italics], but later diminishes and in older patients is very small. He gives the following figures of weight. In 13 patients under 5 years of age the weight was 271 gm.; the average in 25 patients over five years was 65 gm.; average weight in 20 below ten years was 206·8 gm., of 18 over ten years 56·71 gm. In the early stage the spleen is of a dark red colour, the Malpighian corpuscles small and separated. In later stages the organ is small, with a thick, wrinkled, fibrous capsule, small pulp with fibrous trabeculae, and Malpighian corpuscles atrophied, and there are pigmented areas surrounded by giant cells. The arteries have thickened walls, perhaps calcified. The kidneys are congested with sickle cells and the tubule epithelium contains much siderotic pigment. The bone medulla is hyperplasic.

The author notes the parallelism between sickle-cell anaemia and familial haemolytic jaundice: both are familial and hereditary, both

present a haemolytic type of jaundice and destruction of red corpuscles, the type of anaemia and the bone marrow changes are similar; both have haemolytic crises with increase of jaundice and excretion of pigment, diminution of haemoglobin and corpuscle count, and pain in the epigastrium and left hypochondrium, and, finally, both are benefited by splenectomy. [The value of this operation in sickle-cell anaemia is debatable. The author seems to imply that the benefit occurs if the patient is seen early, while the spleen is enlarged.] On the other hand, differing points are the poikilocytosis and the susceptibility to reticulo-endothelial phagocytosis of the red cells, the normal resistance to fragility tests, and the spleen changes. *H. Harold Scott.*

DERMATOLOGY AND FUNGOUS DISEASES.

CELIS PÉREZ (A.). Un caso de cromo-blastomicosis de localización nasal y laringea. [**Nasal and Laryngeal Chromoblastomycosis.**]—*Gac. Méd. de Caracas.* 1943. Jan. 15. Vol. 50. No. 1. pp. 8–10.

The author can find no previous case in which this condition has been localized in the nose and larynx. The patient was a negro, 20 years of age. His nose was enlarged, of "elephantiasic aspect," covered with small nodules (mamelones), scars and ulcers. The patient first noticed a verrucose condition of the exterior of the nose [how long before is not stated] which later ulcerated and satellite nodules and ulcers appeared. When seen by the author these were fairly numerous, but there was no adenitis, no pain and no itching. Laboratory examination proved the lesions to be due to Chromoblastomycosis. The nostrils were almost blocked, but the nasal mucosa was not affected. The mouth and pharynx [the author says 'larynx'—an obvious slip] were normal. As the patient's voice was hoarse the larynx was examined and nodules and granulations were seen on the vocal cords. A biopsy specimen sent to the laboratory was reported upon as "chronic inflammation with granulations and inflammatory infiltration." The Kahn test gave a 4-plus. Antisyphilitic remedies had no effect on the laryngeal lesions. At this point biopsy from the nose showed the true nature of the lesion. Sodium iodide and trypaflavine, with local application of sulphanilamide, were also without effect. Electro-coagulation was then applied, with great benefit. The patient asked permission to leave hospital, promising to return. Needless to say he did not do so and the further progress is not known. The author regards the laryngeal condition as due to the same cause as the nasal, because of the similar appearance and the failure of anti-syphilitic treatment. The condition appears to be one which develops slowly and has little, if any, tendency to generalization. *H. Harold Scott.*

NIÑO (Flavio L.). Ulcera micótica de córnea. Estudio micológico de una observación. [**Mycotic Ulcer of the Cornea.**]—*Bol. Inst. Clín. Quirúrg.* Buenos Aires. 1943. Feb. Vol. 19. No. 154. pp. 115–132. With 3 plates & 14 figs. [18 refs.]

The following is a translation of the author's summary :—

1. A fungus has been isolated from a corneal ulcer which had resisted treatment. A study of this fungus is reported.

2. This study indicates that the parasite is a sporothrix, possibly *Sporotrichum fonsecai* Pereira Filho, 1929.

3. Intensive treatment with iodide, and extirpation of the lachrymal sac, produced definite cure.

4. Ocular sporotrichosis is not common in Argentina, to judge by the literature hitherto published. *C. W.*

MISCELLANEOUS.

MUMFORD (Edward Philpot) & MOHR (John Luther). **Preliminary Report on the Infectious Diseases of Enemy Occupied Territories. Part I: The Japanese Mandated Islands and Guam.**—*Jl. Trop. Med. & Hyg.* 1943. Apr.–May. Vol. 46. No. 2. pp. 15–23. [78 refs.]

This is a detailed account of the diseases of a region for which information is not easy to obtain. There is a long list of references which should be a great help to those wishing to pursue the matter further. The paper cannot well be abstracted, but the information given should be in the hands of those who may have to deal with the medical problems of these islands when they have been occupied by the Allies. *C. W.*

EHRISMANN (Otfrid). Ueber die Verbreitung der Infektionskrankheiten in der Ukraine. [**Infective Diseases of the Ukraine.**]—*Arch. f. Hyg. u. Bakt.* 1943. Vol. 129. No. 1/6. pp. 74–107. With 2 figs. [2 pages of refs.]

This account is too much coloured by anti-Russian propaganda to be taken seriously, but there is a long list of references, which may be useful.

BERRY (W. T. C.). **Nutrition Unit, Medical Section. Second Interim Report.**—*Nyasaland Protectorate Ann. Med. & San. Rep. for Year ending 31st Dec., 1942.* pp. 11–14.

An interim report dealing with tropical ulcer. Lake-shore people cultivating cassava had a profitable year in 1940–41 when shortage of food in the hills drove the hillmen down to buy food. The Lake-shore dwellers disposed of more than they could afford to lose and became short themselves and towards the end of 1941 had to dig up immature cassava of poor nutritional quality; the calorie value was low and susceptibility to ulcers arose. Ulcers have been ascribed to "a diet low in protein, fat, and vitamin B_2 complex, and high carbohydrate." [In the present state of our knowledge it would, perhaps, be wiser, at all events safer, to say "found associated with" rather than "due to"].

Much of the protein normally used was the vegetable protein of maize. In the investigation here reported this was supplemented by lean meat, of which an average daily amount of 1·5 gm. per kgm. body weight was given, raising the total intake to 3–4 gm. per kilo. A group of forty children were given this diet, while two control groups were formed from the nearest villages. The following table gives the number

	Total no. abrasions	Duration in weeks taken for healing													Progressing to ulcer
		1	2	3	4	5	6	7	8	9	10	11	12	12+	
Meat-fed group	288	95	79	41	17	20	9	5	1	5	3	2	1	7	3
Control group I	214	67	50	29	10	8	3	33	—	—	1	1	—	7	5
Control group II	322	115	98	54	20	4	5	17	3	1	2	1	1	—	1

of abrasions observed and the time for healing to take place. [The number in control group I given as 184 should be 214, but this does not affect the accuracy of the rest of the table.]

[It will be seen from this that for quick healing—one week—the control group II was best, 35·6 per cent., the experimental group next, 32·9, and the control group I, 31·3 per cent. ; in the second week the same order is maintained, the respective percentages being 30·3, 27·4 and 23·3. The author states that " there was no obvious improvement in general health, nor was there significant gain in height or weight in the meat-fed group." There would, therefore, seem to be no advantage gained from the increased protein.] Vitamins A and C are available in most abundance at the height of the ulcer season. Bacteriologically, in December to April, *i.e.* during the rainy season, 22·8 per cent. of 381 abrasions showed fusiform bacilli ; during the rest of the year only 7·9 did so. [More investigation is clearly needed to elucidate the causes and reasons for prevalence of tropical ulcers in Nyasaland.] *H. Harold Scott.*

BASU (Arun Kumar). **Endemic Tropical Ulcers (Naga Sores) among the Coolie Recruits in the Jungles of Assam.**—*Jl. Indian Med. Assoc.* 1943. Mar. Vol. 12. No. 6. pp. 161–165.

The ulcers described are common in those working in damp, steamy jungles, as in Assam, Cochin China, Malaya, Melanesia, for example. The author's cases, ten of which are described, were among coolies recruited from Singhbhum district to work in Assam. In some the ulcers developed while they were on their way home. They were nearly always on the legs and feet and started as small hard, pink papules which within 48 hours became vesicles and broke, discharging blood-tinged serum and forming an ulcer, at first shallow, then extending superficially and in depth ; occasionally they were multiple and fusion would take place. Two patients died after the ulcers became septic and gangrenous. Fusiform bacilli and Gram-positive diplococci were seen, but not Leishman-Donovan bodies. Experimental inoculation into a skin wound showed that the condition was infective ; application of the discharge to uninjured skin did not give rise to any lesion.

The usual methods of treatment of ulcers by disinfectants, formalin, mercurial ointments, etc., proved ineffectual. The following, however, gave very satisfactory results : The patient was put to bed and the limb immobilized by splints ; the ulcer was cleaned with E.C. lotion

[nowhere does the author give a hint as to what E.C. stands for, which is unfortunate as others might like to try the treatment in intractable tropical ulcers], or, if the discharge was great, the leg was placed in a bath of it for half-an-hour and rectified spirit applied to the ulcer and around it. It was then dressed with 2 per cent. tartar emetic ointment and bandaged. Later the strength of the ointment was doubled. Urea stibamine was given intravenously on alternate days, starting with 0·05 gm. in 10 cc. of 25 per cent. glucose solution, increasing to 2·0 gm. Cod liver oil was given twice daily. Cure was usual in a fortnight. [There would naturally be a desire to obtain a cure as rapidly as possible, but it seems a pity that the tartar emetic, the urea stibamine and cod liver oil were all employed together, for it is impossible to tell which was mainly responsible for the happy result.]

H. Harold Scott.

HENDERSON (J. M.) **The Relation of Sunlight to Desert Sores.**—*Brit. Med. Jl.* 1943. May 29. pp. 657–659.

In appearance and course, desert sores were quite different from furuncles and from septic sores following chafing, insect bites or epidermophytoses. The individual lesion started as a "water blister," 2 to 10 mm. in diameter, itching sometimes being felt before the blister appeared, although when the vesicle was fully formed there was neither itching nor pain. After 12 to 24 hours the blister ruptured and the lesion then developed into a purulent spreading subepithelial "whitlow" (*sic*), 1 to 3 cm. in diameter, which was resistant to treatment, some 2 or 3 weeks elapsing before healing was complete; occasionally there was an associated low grade lymphangitis or adenitis. The lesions were multiple and when a patient presented himself for treatment it was not uncommon to find vesicles forming, as well as developed sores. Out of 50 patients 12 had coincident impetiginous lesions of the face, but the fluid from the initial blister of the desert sore appeared sterile and produced no reaction on intradermal inoculation into a normal person. Although trauma may have played some part in determining the site of certain of the lesions, many sores occurred on areas where there had been no injury and in 21 of the 30 patients there was no history of trauma. It is suggested that the chief aetiological factor was the action of sunlight, aided perhaps by slight trauma on skins reacting badly to exposure to the sun. The sores occurred only on those areas of the limbs exposed to the sun and chiefly in persons whose power of adaptation to sunlight was below the average and whose skin reacted to exposure, with erythema, dryness and scaling. Cases appeared almost in epidemic form at the beginning of the desert summer, their incidence seemed to have no correlation to the time that the individual patients had spent in the desert, and in patients who had more than one attack the sores appeared only during the summer months. While the effect of a vitamin deficiency could not be discounted, the absence of any of the features of scurvy seemed to indicate that vitamin C was not involved, and it was also reported that similar sores occurred in troops receiving adequate amounts of fresh food. [Other observers have, however, felt that the incidence of desert sores may have some significant connexion with the absence of fresh fruit or vegetables.] It is suggested that the susceptible type of person should wear clothing adequate to protect against sunlight and that a vanishing cream or oil,

preferably containing a small amount of antiseptic, might be helpful. Some men, in the absence of a medical officer, found germolene and elastoplast useful in treatment of the sores. *F. Murgatroyd.*

LEEDHAM-GREEN (J. C.) & EVANS (Winston). **Myositis Tropica.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1943. May. Vol. 36. No. 6. pp. 359–362.

The authors describe briefly the characteristics of 20 cases of tropical myositis, all in natives ; 11 were from Nigeria, seven from the Cameroons, and two from the Gold Coast. All presented tender swellings, which might be circumscribed or diffuse, and involved the limb muscles. The temperature was not as a rule high, usually 101°–102°F. occasionally a degree higher. In one case, described in detail, there was a leucocytosis of 11,000 per cmm. Pus was found on incision in five of the patients, and *Staphylococcus aureus* was isolated. In others, although heat and fluctuation were present, incision released no pus, but, on microscopical examination of tissue removed by biopsy, the muscles involved were glassy and oedematous ; there were loss of striation and monocytic infiltration of the interfibrillar connective tissue, with fibroblastic reaction around the necrosed area.

[There is probably, nay certainly, more than one form of myositis in the tropics ; that described by the authors they consider to be "an acute degenerative condition, characterized by haemorrhage into the intermuscular tissue spaces together with a mononuclear cell infiltration, producing an appearance similar to the coagulative necrosis of muscle (Zenker's degeneration)." They offer no suggestion as to aetiology of this curious condition. See this *Bulletin*, 1942, Vol. 39, pp. 348, 894 ; 1940, Vol. 37, p. 225, where numerous other references are cited.] *H. Harold Scott.*

MACLEAN (Kenneth S.). **Observations on Sunstroke and Heat Exhaustion in the Tropics.**—*Jl. Roy. Nav. Med. Serv.* 1943. Jan. Vol. 29. No. 1. pp. 31–36.

Of 21 patients suffering from conditions directly attributable to heat, in the crew of a cruiser, only one showed hyperpyrexia ; the remainder suffered from heat cramps (fireman's cramps). The symptoms of heat cramps are :—the muscular pains from which the condition takes its name, headache, vomiting, dizziness and, sometimes, rapid, panting respiration. Collapse and death may occur if treatment is not given. In some cases, however, the patient may complain of headache, nausea and dizziness only ; in most cases the temperature is normal. Cases in which cramps occur should always be regarded seriously.

It is known that cramps are due to excessive loss of chloride during profuse sweating, and firemen have long realized that cure lies in the drinking of water to which common salt is added. Administration of salt was therefore the basis of the author's treatment, and proved highly successful ; 2 pints of water, containing 2 drachms of salt, were taken in sips during each 24 hours. In addition, 8 pints of sweetened fluid, to which 1 drachm of sod. bicarb. was added, were taken each day. In severe cases, or when vomiting occurred, rectal or intravenous salines were given.

The author, however, was not satisfied with the treatment of cases in which the condition had developed, and turned his attention to methods of prevention. Ship's water, distilled at sea, contains little or no sodium chloride ; an " epidemic " of 14 cases occurred after 12 days at sea. He therefore instituted the following procedure :—

" (1) One lb. of salt per diem was added to the distilled water for every 350 men carried. Assuming that 10 per cent. of this is drunk, this ensures that on an average each man gets 20 gr. of salt per day as a basic ration. In addition men are instructed to add at least half a teaspoonful of salt to their drinking water each day (*i.e.* an additional 30 gr.).

" (2) All ratings keeping watches below should take half a teaspoon of salt in a pint of water every time they go on watch.

" (3) Everybody was instructed to take a teaspoonful of salt in a pint of water immediately they felt the slightest ill-effects such as nausea, headache, or dizziness after working below or being in the sun. Provided the water is ice-cold this is quite a palatable drink."

A description is given of a case of hyperventilation tetany in a man who showed signs of heat exhaustion ; the theory advanced is that deficiency of sodium chloride in the body may irritate the respiratory centre. *C. W.*

TREU (Rudolf). **Pseudo-Tuberculosis of the Lungs with Eosinophilia : Contribution to Treatment.**—*Indian Med. Gaz.* 1943. Feb. Vol. 78. No. 2. pp. 70–71. With 5 figs. on 1 plate.

Two cases of so-called " eosinophile lung " are here recorded, but, as an Editorial note aptly states, " It is difficult to see how the diagnosis in this [the second] case is justified ; ' idiopathic eosinophilia ' is very common in this country." The cardinal symptoms are infiltrative processes in the lungs with fever, cough, and sputum, which is free from *Myco. tuberculosis.* Another important point is that the first patient reported here was a European, 41 years of age. He stated that for 6–8 weeks he had had a cough, specially troublesome at night, a temperature to 101°F. or more, he felt weak and had lost more than 20 lb. in weight. Physical signs resembled those of bronchitis and asthma, X-rays showed an evenly distributed mottling. Blood sedimentation was rapid, 24 minutes ; there was a leucocytosis of 23,400, of which 82 per cent. were eosinophiles. After other drugs had proved ineffectual, the patient was given acetylarsan, 1 cc., 2 cc., 3 cc., intramuscularly on alternate days, and thereafter 3 cc. every third or fourth day till a total of 36 cc. had been administered. After about four weeks, the sedimentation time was two hours, and three weeks later the leucocytes had fallen to 6,250 and eosinophiles to 8 per cent. Two months later, after a visit to South Africa, the patient was again examined and the eosinophiles were only 4 per cent., and he said he felt quite well ; he had regained his normal weight and X-rays revealed no abnormality.

The second patient presented somewhat similar symptoms, but he had also signs of old tuberculosis in the lungs. His treatment with acetylarsan was interrupted by an attack of lobar pneumonia and on recovery from this the other condition had also cleared up, and the eosinophilia which before treatment was started was 72 per cent. of a total leucocyte count of 38,600, had fallen to 4 per cent. in a normal blood picture. *H. Harold Scott.*

PRIETO CASANOVA (José T.). Contribución al estudio de los infiltrados pulmonares fugaces. [**Transient Infiltration of the Lungs.**]—*Rev. Policlinica Caracas.* 1942. Nov.–Dec. Vol. 11. No. 67. pp. 323–356.

This is a very full account of the condition, some cases of which at least go by the name of Loeffler's syndrome [see this *Bulletin*, 1941, Vol. 38, p. 538]. In the course of examination of 1,173 persons, 998 adults and 175 children, 33 cases were found (2·8 per cent.) ; 18 were among the adults (1·8 per cent.) and 15 among the children (8·5 per cent.). The sex proportions were, among adults, females 11, males 7, among children, 11 and 4 respectively.

The author defines the condition in the following words [translated] : " Transitory pulmonary infiltration is [shown by] a shadow discovered accidentally on X-ray examination, without symptoms, transient and benign." X-rays may show clouding, or pneumonic, bronchopneumonic or reticular shadows. He makes no mention of the eosinophilia as a characteristic because, he maintains, this is met with in a certain group of cases only.

Causes to which the condition is attributed are many ; among them influenza, asthma, tuberculosis, diphtheria or other infectious fevers—scarlet fever, measles, whooping cough—parasitism generally, especially helminthic, allergy to the pollen of *Liguntum vulgar*, or a combination, such as influenza and ascariasis, tonsillitis and the same worm, and so on, the transient migration of the Ascaris larvae causing the infiltration.

The author adopts the following classification : (1) Transitory tuberculous infiltration. (2) Typical (according to the definition). (3) Atypical. The first he regards as a toxic or allergic manifestation in a tuberculotic. The second includes the Loeffler syndrome, asthmatic and allergic cases and those of parasitic origin. The third includes those associated with influenza, or pneumonic or bronchopneumonic foci. Blood examination in 22 cases showed :—no eosinophilia (3 per cent. or under) in three, moderate (5–15 per cent.) in eleven, and over 16 per cent. in eight. Corpuscle sedimentation was usually normal in rate, but occasionally slightly increased. *Myco. tuberculosis* was looked for in 23 patients, but was not found in any. Faecal examination of 19 subjects yielded no parasites in 9, ova of Ascaris in 4, of *Schistosoma mansoni* in 1, Trichuris in 2, and cysts of *E. coli* and *E. histolytica* in 3, but only one examination was made in each case. He concludes that : (1) The condition is fairly common in Venezuela. (2) It may be provoked by parasitism (Ascaris, Schistosoma), infection (influenza, tonsillitis), allergy (asthma), bacteria (*Myco. tuberculosis*). (3) Symptoms bear no relation to the extent of lung involved ; the condition is usually found by chance, when symptoms are slight or absent. (4) Eosinophilia may be present, but in some the proportion is normal. (5) Prognosis is good except in tuberculous patients. [We have dealt with this article fairly fully because it is a genuine attempt to throw light on an obscure question, but we feel bound to add that from the evidence adduced mere concomitants have been raised to aetiological status on insufficient grounds, and that the number of cases is far too small to enable such wide generalizations to be drawn.]

H. Harold Scott.

BRULÉ (Marcel) & PESTEL (Maurice). Intoxication par les fèves et hémoglobinurie. [**Favism and Haemoglobinuria.**]—*Presse Méd.* 1943. May 8. Vol. 51. No. 18. pp. 241–242.

Two cases of this curious disease are briefly noted; a brother and sister, aged 18 and 15 years respectively, were suddenly attacked by jaundice and the passing of blackwater. The elder died in five days with anuria and azotaemia, the younger recovered rapidly and completely. The condition was thought to be paroxysmal haemoglobinuria *a frigore*, but the mother made much of the fact that the day before the onset they had both eaten heartily of a meal of bean-flour and that a month before they had both had a sudden attack of jaundice after a similar repast.

The rest of the paper is taken up with a general account of favism. It is common along the Mediterranean, in Southern Italy, Corfu, Greece, northern Egypt, and is caused by ingestion of the meal or inhalation of the flowering plant. Only certain members of a party or family eating the food (commonly broad beans, *fève des marais*) are attacked and there is little doubt that allergy plays a part, probably a large part, in producing the symptoms. [More ought to be known of this as a cause of haemoglobinuria. An excellent account of it is given in Stitt's *Tropical Diseases*, 1942, Vol. II, p. 1202, see also this *Bulletin*, 1942, Vol. 39, pp. 279, 639.] *H. Harold Scott.*

GENEZZANI (U.). **Bean Disease (Favism).**—*Harefuah.* Jerusalem. 1943. Mar. 15. Vol. 24. No. 6. [In Hebrew pp. 95–97. English summary p. 97.]

MONTEL (R.). Accidents dus à l'impact des filaments pêcheurs de certaines méduses des mers tropicales aperçu sur ces Coelentérés. [**Accidents due to Contact with Medusa Rays.**]—*Bull. Soc. Path. Exot.* 1942. Apr. 22 & May 13. Vol. 35. Nos. 4–5. pp. 168–176.

The patient, a doctor, was bathing at Longhai, Cochin-China, when he suddenly felt a sharp pain, like a burn, in the left axilla, upper arm and side of the chest. The Annamite fishermen told him on his reaching land that he had been stung by a "sua lua," a Medusa or jelly-fish. The pain was severe and half an hour later he had difficulty in breathing, with a feeling of constriction of the chest, and he became cyanosed. This was succeeded by pain of much severity, with remissions, in legs and feet, and tremors of legs and arms. These symptoms lessened but were still present eight days later. He also suffered from nausea, meteorism, gastric crises and laryngeal irritation with irrepressible troublesome cough which prevented sleep, expectoration and great weakness, accompanied by marked restlessness and a sense of impending death. Rhonchi and sibilant râles could be heard at both bases behind. There was marked albuminuria. Treatment consisted of cupping the chest, injection of "antivenin C" (20 cc.), ephedrine, camphorated oil, stimulants, etc.

The tentacles of these Medusae have special cells, cnidoblasts, enclosing nematocysts or small sacs with invaginated neck continued as a coiled spiral hollow filament in a toxic fluid. On contact of a foreign body with these cysts, the filament is ejected and pierces the skin, injecting the toxin. According to BESREDKA, the intensity of the

symptoms depends on the number and extent of the points of contact; the chief symptoms are reduction of arterial tension, acute emphysema and bronchial spasm, and stimulation of the vagus, and the lung is the seat of intense bronchial reaction and exudation with vasoconstriction. *H. Harold Scott.*

WILSON (H. T. H.) & ELLIS-JONES (D. W.). **A Case of Acute Dermatitis occurring after handling Pyrethrum Powder, with Treatment.**—*East African Med. Jl.* 1943. Mar. Vol. 20. No. 3. pp. 89–90.

The use of pyrethrum as an insecticide is so widespread and cases of susceptibility to it so rare in comparison that the recording of this case is of no little importance. Use of the spray of pyrethrum powder caused irritation of the hands. The use of it again the next day was followed by itching and transient erythema. On the third day the patient used it for a longer period, about half an hour, and his hands became acutely inflamed, with a vesicular erythema of the fingers, palms and front of the wrists. Within a week he had to be admitted to hospital on account of swelling of the hands and a red oozing from the skin and extension of the erythema. A little relief was obtained from local application of calamine lotion, but again the lesions flared up: the arms and face became oedematous with desquamation in patches. Much benefit was obtained from intravenous injection of 0·5 gm. sodium thiosulphate in 10 cc. water at five-day intervals, but the rash did not clear altogether till three months after the initial lesion appeared. *H. Harold Scott.*

DASTIDAR (S. K. Ghosh). **A Study of Tetanus and its Treatment with Magnesium Sulphate.**—*Indian Med. Gaz.* 1943. Feb. Vol. 78. No. 2. pp. 73–79. With 3 figs. [11 refs.]

The author's method of treating tetanus patients is to administer 25 per cent. magnesium sulphate solution intramuscularly in doses of 5 cc. to adults, 2–4 cc. to children and adolescents, twice daily, with injection of antiserum, 9,000 units, repeated in 48 hours, and, if convulsions are severe, morphine grain 1/4 and atrophine grain 1/100; glucose, 50 cc. of a 25 per cent. solution, was administered intravenously after each injection of morphine.

The author analyses 155 cases admitted to hospital [he mentions 211 in his summary, but excludes 56 cases of tetanus neonatorum from his discussion] from the aspects of sex, age, incubation period in general and its relation to site of injury, and mortality rates. The number is too small for valid deductions and the argument is at times rather arbitrarily selected. For example, as regards sex incidence, 86 were males and 69 females, but "the incidence in the males would appear to be nearly 2·3 times more than that in the females." This ratio is arrived at by excluding 31 cases in which the infection was acquired during or just after parturition.

It can be stated, however, that the magnesium sulphate injections seemed to control the convulsions and did not produce any ill-effects. The intramuscular route was chosen because intrathecal injection was not practicable, intravenous injection is dangerous and may cause

sudden failure of respiration, while subcutaneously the solution causes much pain. [For its use in tetanus neonatorum see this *Bulletin*, 1927, Vol. 24, p. 493]. *H. Harold Scott.*

PEARMAN (R. O.) & HASEMAN (L.). **Cochliomyia Americana Infestation in Man. Case Report.**—*Ann. Surgery.* 1943. Mar. Vol. 117. No. 3. pp. 468–472. With 2 figs.

BOOK REVIEW.

ALLEN (Paul H.). **Poisonous and Injurious Plants of Panama.**—*Supplement to Amer. Jl. Trop. Med.* 1943. Jan. Vol. 23. No. 1. 76 pp. With 19 figs. & 1 plate. [Bibliography.]

The author's object in writing this brochure on the Poisonous and Injurious Plants of Panama is very sound. Of the thousands of United States troops now enlisted a large proportion are concentrated in the Canal Zone district where they are constantly exposed to the temptation of Adam and Eve to eat of forbidden fruit. Hitherto they had perhaps some excuse for the Fall, for they did not know it was forbidden, but after reading what the author has written they can no longer plead that they have not been warned. All cannot read it, but all medical officers should make a point of doing so and they should then give talks to the officers and men whose health is entrusted to them, and the value of such a talk would be much enhanced by an exhibition of the poisonous plants. Meanwhile, the general advice to "avoid using any jungle fruits or seeds for food unless *very sure* what they are" should always be borne in mind.

Criticism is disarmed when the author acknowledges that his work is "probably guilty of many sins both of omission and of commission" and asks readers to notify him of points calling for correction or amendment. "It is hoped," says the author, "that this beginning may stimulate interest in the subject." There is no doubt that it will accomplish this, and it is hoped that it will stimulate research into the toxic principles which in many cases are still undetermined, and it is not improbable that some at least may prove a source of medicinal preparations.

More than a hundred plants are mentioned. It must have been difficult to find a satisfying classification, but, in the opinion of the reviewer, that chosen is probably one of the least satisfactory, in fact in the true sense it is not a classification at all, some being grouped according to the symptoms they produce, others according to structure and properties, and a third group as accidentally harbouring parasitic insects. Most "Stomach Poisons" will cause purging as well as emesis; hence, to separate into two large groups, A, Stomach poisons

(in which 36 are described) and B, Purgatives and Emetics (10 described) leads to much overlapping and not a little needless confusion. Next comes a group of 32 Vesicants and Irritants, which is separated from a fourth group of 14 Urticants, although an Urticant is an Irritant and may be a Vesicant. Again, this leads to an arbitrary severance of members of the same Genus. For example, *Thevetia nitida* is described in Group A, Stomach poisons, while *Thevetia neriifolia* is to be found among the Vesicant and Irritants in Group C. *Solanum mammosum* and *S. nigrum* come under Stomach Poisons, *S. tuberosum* under another group 14 pages later. This is justified by the fact that the fruits of the former are toxic, whereas it is the tuber of the last. One more example will suffice. Under *Andira inermis* we find " The attractive pale purple flowers produced in terminal panicles. . . . The fruit is globose. . . . The bark in large doses is a dangerous poison, and the seeds are said to contain a dangerous alkaloid." Unless the United States soldier is more highly educated than most this description will convey little to his mind ; also, no soldier is likely to eat the bark in large doses and, though the seeds are poisonous, there is no mention of the plant under this subjection in either group A or B. Similarly, under *Mirabilis jalapa* " The roots . . . have drastic purgative properties. The rough black seeds . . . are also poisonous if eaten." This is grouped under Roots and Bulbs, but surely the passer-by would be more likely to chew the seeds than eat the roots.

If the present classification is retained, for purposes of reference an Index is a necessity, for one has to look through from the beginning to find any one poisonous plant. If there is no Index, then the alphabetical order would be more convenient.

The publication is very helpful and complete in giving the local names for the plants among the different peoples of the Caribbean. The work is, in the main, a botanical description of each of the plants —in fact, it is little more. The symptoms they produce receive but a word or two here and there, without details (except in the case of *Nerium oleander*) and treatment which, after all, is most important, is not touched upon.

Information on *Manihot utilissima*, a plant used extensively for its starch, for making tapioca and cassava cakes, receives scanty mention. That all varieties " possess a greater or less percentage of hydrocyanic acid " is not quite correct. They are cyanogenetic, that is, they contain a glucoside and an enzyme and on contact with water these react to form hydrocyanic acid ; hence, the first two or three washings are always thrown aside. In other places the author might well be more dogmatic and less cautious than he is. Thus, " all parts of the plant [*Jacquinia panamensis*] *seem* [our italics here and below] to be used as fish poisons." They either are or are not ; it should be easy to prove. " The poisonous principle [of *Abrus precatorius*] is *reported* to be Abrin " and, again, " The poisonous principle [of *Ricinus communis*] *seems* to be due . . . to Ricin." He means the symptoms produced are due to the principle, and in each case the fact is *known*, the principles are abrin, ricin, which, with crotin and robin, are phytotoxins. The abrin, states the author, " seems to be confined to the coating of the seeds." Whereas the ' needles ' of the crushed seeds have been well known, in the East for a long time, to be intensely poisonous when they penetrate the skin and they have been used for homicidal purposes and for killing cattle. There is little or no danger from swallowing the seeds.

When writing of *Hippomane mancinella* the author devotes two lines to the fruit and half a page to the risk of cutting the trees and working with the wood. The danger for the ordinary man is the fruit ; hundreds of cases of poisoning have occurred among sailors who, on landing, plucked and ate the tempting apple, and suffered consequently from blistering and erosion of the mouth and tongue and from nausea, vomiting and dysphagia. OVIEDO (1478–1557) noted the temptation to eat the fruit and the author uses Eden's translation of his remarks on this as facing to the frontispiece.

The brochure is embellished with a score of excellent illustrations, but there is no indication of the relative size of the photograph to that of the natural object, though notes of dimensions are made in the text. There is a brief bibliography.

Is it too much to ask the author to expand this excellent preliminary work and tell us of the research carried out on the toxic principles involved and initiate work on many at present obscure or unknown ? Such a work would form a standard treatise on Tropical Toxicology. It would be a life-work and, in the meantime, as a relaxation or less arduous task, we would like to see a fuller account of the symptoms produced by the poisonous plants he has described, the indications for and the details of treatment, and the pathological lesions in fatal cases. The present work is written in an engaging style and even in its present form is to be recommended for wide distribution among those stationed in Panama and the Canal Zone. *H. Harold Scott.*

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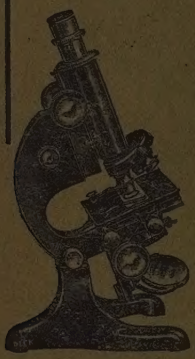

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